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THALAMIC ACTIVITY IN STUPOR

BY

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WHILE studying the electrical activity which arose in the substance of the cerebral hemispheres in patients with abnormal behaviour, we came across unique disturbances in the optic thalamus of a man who was akinetic and mute. These disturbances were rhythmic, they recurred frequently and they were related to the electrical changes in the cortex. They were present when the man was stuporose but not when he was normal—a fact that was confirmed on repeated recording. Similar thalamic disturbances were later found in a second case of the same type. As the changes in the brain function which cause akinesis and mutism are not known, the phenomena were studied in some detail. In this paper the facts obtained upon the two cases by clinical and experimental methods are recorded and discussed. The paper was communicated to the International Congress of Neurology, in Paris, 1949.

The term stupor in the title is used as being synonymous with the phrase "akinesis with mutism," for comparison shows that the clinical state called stupor by psychiatrists is the same as neurologists' "akinesis with mutism." When the words akinesis and hypokinesis are used alone, they usually refer to the condition seen in parkinsonism, while the word mutism alone is commonly reserved for the condition found in deaf mutes. Neither "stupor" nor "akinetic mutism" imply ætiology, for both are descriptive—apparently of the same condition. They have in common a clear distinction from states of impaired consciousness—confusion, semicoma, or coma. Although the term stupor has been used uncritically in this regard, since it comes off the tongue so easily when an unresponsive patient is seen, it seems the more desirable term to use in this paper so long as it is accepted to mean akinesis with mutism. The results refer to electrographic records made simultaneously from different points in the thalamus, the subcortical white matter, the cere-

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bral cortex, and from points on the scalp. The method employed was detailed by us in this Journal (Williams and Parsons-Smith, 1949) when the findings in other conditions in comparable circumstances were described.

Case I.—St. George's Hospital Case No. 95926.

This man of 39 was admitted to the Neurological Department in November 1947 and again in November 1948. On each occasion he was admitted urgently in a state of akinetic mutism, from which he made a full recovery after some weeks, on each occasion. The investigations which are described here were undertaken two years ago, during his second period under our care.

History.—He had had good health and had had no injuries, faints, fits, or symptoms of disorder of the nervous system. No relevant points arose in his family history.

On November 30, 1947, he was admitted apparently in coma having had a series of epileptic convulsions that day. His wife said that he had not been well for six months and had lost his usual energy and interest.

On November 23 he woke with a right frontal headache, which recurred each morning. On November 29 he had difficulty in dressing himself as he seemed unable to understand how to get into his clothes, and he was abnormally slow in his actions. Later he seemed dazed and was clumsy. Next morning he had four fits in which the left side of the body twitched first, followed by generalized clonic movements when the tongue was bitten.

Throughout the day he was dazed, did not speak and did not appear to recognize anyone. He was incontinent.

Mental state.—When admitted to hospital he was recumbent and immobile. When first seen he was lying motionless and immaculate as he had been arranged by the nurse. The bedclothes were being disturbed by quiet breathing, and his expressionless face by an occasional blink. His eyes were open and he seemed to be looking at the ceiling. Not only was there no spontaneous movement, but he did not respond to questions or commands in any way at all. Yet he was clearly not in coma. As he paid no attention to speech, noises were made but he was not startled, so slight pain was inflicted with a pin. There was again no response, either by change in expression, in speech, in pulse, in respiration, pupillary size, or by movements of the limbs. When the pin-pricks were continued and increased in severity he then tried to restrain the examiner as a normal man would, by pushing away the hand which held the pin, and not by rubbing or scratching the tormented area, or by making ineffectual protesting movements as would a man in coma. This purposive response to extreme stimulation, together with the blinking of his seemingly alert eyes, his normal quiet respiratory rhythm, his facial expression and the total absence of any movement apart from respiration, distinguished this state of akinetic mutism from coma. He remained helpless and incontinent.

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On detailed physical examination the following abnormalities were found:

The pupils were equal, circular, small but eccentric. They were fixed to light. From time to time the eyes spontaneously deviated to either side, the axes being parallel. Within the limitations of the examination imposed by the patient's state the cranial nerves were in other respects normal. In particular the optic discs were quite normal. No abnormal movements occurred in the limbs. There was generalized hypotonia, the reflexes being equal and sluggish. The abdominal reflexes were absent, the plantar responses flexor. Other systems were normal except for the blood pressure which was 220/110.

In view of the akinesis, mutism, abnormal pupils and hypertension the patient was thought to have a lesion in the neighbourhood of the third ventricle.

The following investigations were performed:

1.12.47: X-rays of the skull were normal. The pineal gland lay in the mid-line. Ventriculography was performed by Mr. Wylie McKissock. Both lateral ventricles and the third ventricle were normal in size, shape and position. There was no deformity of the aqueduct.

The C.S.F. was under normal pressure. It contained 1,000 red blood corpuscles and 20 polymorphs per c.mm. There were 10 mg. protein and 700 mg. chlorides per c.c. The Wassermann reaction was negative. Lange curve—no change.

Blood count: Red blood corpuscles 5,200,000; hæmoglobin 102 per cent; white blood corpuscles 20,000; polymorphs 80 per cent, lymphocytes 18 per cent; monocytes 2 per cent.

Blood Wassermann reaction negative.

Routine urinary examination: No abnormality.

Electroencephalogram 1.12.47: Was grossly abnormal. High voltage rhythmic discharges consisting of 3- and 6-a-second waves coupled together (fig. 1) arose in both hemispheres but were more evident in the right, and there was suppression of the normal frequencies. The discharges were widespread throughout the hemispheres, and were associated with rhythmic 1-a-second waves. Although the right side was the more abnormal no evidence of a local lesion could be seen. Records of this sort had previously been seen in cases of virus encephalitis involving the mesencephalon, and this diagnosis was suggested.

Progress.—1.12.47: Five major convulsions, beginning and ending in the right arm. When he recovered he was following objects with his eyes. Incontinent of urine and fæces.

2.12.47: Conscious but inactive and silent, condition unchanged, incontinent. B.P. 190/110, T. 99·4° F.

4.12.47: Speaking for the first time, in simple requests. B.P. 170/110.

8.12.47: Now restless answers questions simply; incontinent. B.P. 180/120.

12.12.47: More alert, co-operative and rational. No longer incontinent. B.P. has fallen to 130/75. Pupils now equal, dilated central, reacting to light, but poorly to accommodation. More detailed examination of the nervous system was now possible. Abnormalities found were loss of upward deviation of the eyes; a complete left homonymous hemianopia; equal but sluggish tendon-jerks in a motor system which was in other respects normal. Blood count—W.B.C. have fallen to 7,000 with the same differential proportional count.

Electroencephalogram 18.12.47: Has improved since the recording on 1.12.47. The records now show virtual absence of any dominant frequency with symmetrical runs of low voltage 5-a-second waves occurred in all leads.

There was no evidence of any local focus of abnormality, and no characteristically "epileptic" discharges were recorded (fig. 1).

6.1.48: The patient continued to improve in all respects.

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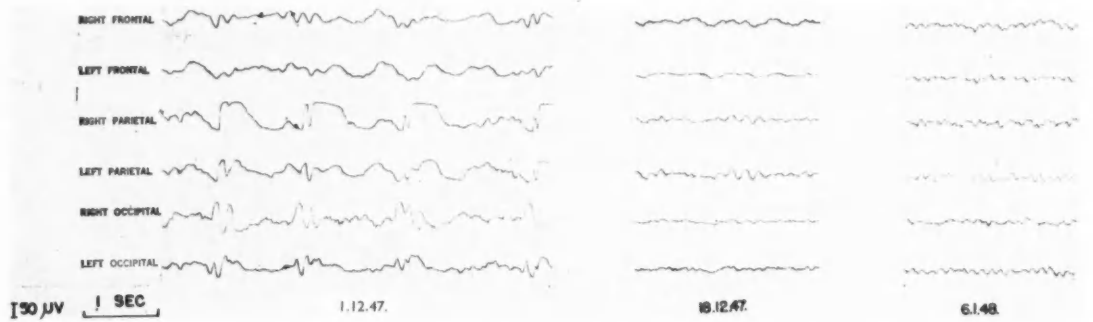

FIG. 1.—Electroencephalograms recorded on Case 1 on first admission to hospital. The peculiar rhythmic wave complexes in the first records should be noticed. These complexes recurred at intervals of about 1·5 sec. and were more evident in the right side. They seem to be peculiar to patients with bilateral high mesencephalic lesions, and are commonly seen in encephalitis. The subsequent records show a steady improvement, so that in the last series normal alpha rhythms can be seen.

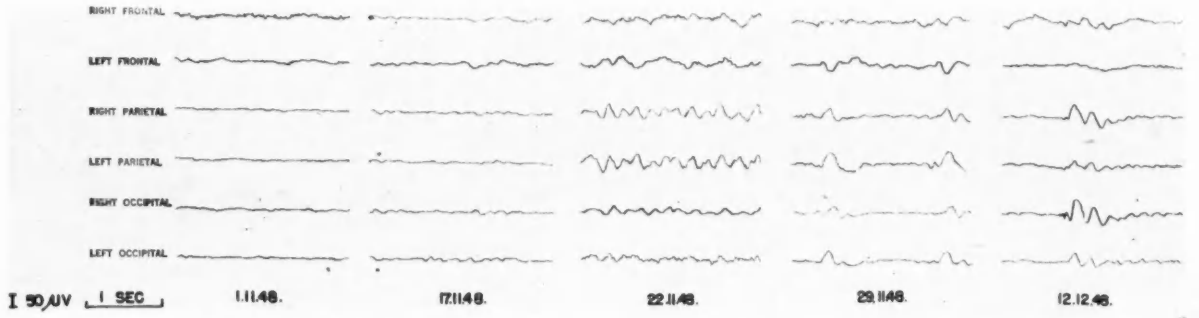

FIG. 2.—Electroencephalograms recorded on Case 1 on the second admission to hospital. They show the marked differences which occurred from day to day which are described in the text. The initial records were flat, but later episodes of waves and rhythms of 3-a-second occurred throughout both hemispheres.

Electroencephalogram 6.1.48: There had been great improvement in the records since 18.12.47. There is now a dominant frequency of 8-a-second which was previously absent. There are still low voltage 3- to 5-a-second waves in the hemispheres (fig. 1).

18.1.48: The patient was ambulant and his activity unimpaired. His speech was fluent. Except that he had a left homonymous hemianopia with macular sparing, he had no abnormal signs in his central nervous system. The intra- and extra-ocular movements were full. Psychometric testing showed a slight defect of topographical memory and visual constructive capacity which was considered to be a residuum of a right parieto-occipital lesion.

Electroencephalogram 3.2.48: Showed that there had been further improvement in the next three weeks. The alpha rhythm was more persistent and of much higher voltage. There were still episodes of rhythmic 7- to 8-a-second waves, but these were the only abnormality detected.

Readmission (29.10.48).—The patient's recovery had been steadily maintained after discharge from hospital and six months before readmission he had returned to full employment. The day before this readmission he had three generalized convulsions.

Mental state.—On the day of admission he was in a peculiar and variable mental state which at first was thought to be due to three recent convulsions, but which in fact continued for the next four weeks.

His state would vary from hour to hour. At its worst he lay or sat without any spontaneous movement of the face, trunk, or limbs and was absolutely mute. At the best he was monosyllabic and passive.

When examined in his akinetic state the eyes were open, he would blink, and all automatic and reflex movements were normal. He would also move his eyes to a moving object. There was no catatonia or flexibilitas cerea. When more normal there was a great poverty of spontaneous movement, but he would move to command and on stimulation. He answered questions in monosyllables with short simple sentences, and when he did so it was clear that he was disorientated in space and time, and had no memory for recent events. He could not recall any particulars about himself or his family. When able to co-operate more fully he appeared to be dysphasic and dyspraxic, but we concluded that this was simulated by a true error of symbolic understanding. Occasionally the patient would change from a state of complete akinesis and mutism to one approaching normality in a moment, and then would as rapidly return to his former condition. Physically he was normal except for the residual hemianopia, defect of upward deviation of the eyes, and sluggishness of the tendon-jerks. The blood pressure was 130/80. He was febrile.

Investigations.—Urine: Contained sugar but no acetone bodies.
Blood count: No abnormality.
Erythrocyte sedimentation rate: First hour 5 mm.; second hour 18 mm.
Blood sugar (fasting) 180 mg.
Glucose tolerance curve (50 grammes glucose): ½ hour 220 mg.; 1 hour 280 mg.; 1½ hours 300 mg.; 2 hours 260 mg.

were flat, but later episodes of waves and rhythms of 3-a-second occurred throughout both hemispheres.

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Lumbar puncture: Pressure 120 mm. C.S.F. normal in appearance. Contents—10 red and 5 white corpuscles. 10 mg. protein per c.mm. Sugar and chlorides normal. Wassermann and Kahn reactions negative.

X-rays skull again normal. Pineal gland in the mid-line.

Ventriculogram 12.11.48: "The third ventricle and septum pellucidum stood erect in the mid-line. The lateral ventricles were dilated. The right lateral ventricle measured 2·7 cm. compared with 2·4 cm. at the last examination, and the left 3·1 cm. compared with 2·6 cm. they lay in normal position, the third ventricle was in normal position and aqueduct and fourth ventricle were filled and were normal (fig. 3). Conclusions: There is hydrocephalus of the lateral ventricles which was not present in the previous pictures. No expanding lesion was found. This dilatation may be due to cerebral atrophy" (Dr. J. W. D. Bull).

Electroencephalogram 1.11.48: "The records are very flat throughout, showing none of the 'epileptic' disturbances or of the characteristics seen in the previous recordings. There was no evidence of local brain disorder, but the normal rhythms which returned so dramatically ten months ago have again disappeared" (fig. 2).

Electroencephalogram 22.11.48: "The records were again flat, with an unstable dominant frequency of 9-a-second of low voltage. Clear-cut 'epileptic' discharges of 5-a-second appeared in the hemispheres, but were more evident on the right side" (fig. 2). They were recorded again on 29.11.48 and 12.12.48.

Progress.—The variable state of akinesis and hypokinesis continued without any other evidence of disease of the nervous system. He was placed on 10 units of insulin twice a day, and a 210 grammes carbohydrate diet. Control of the diabetes did not affect his mental state.

29.11.48: Marked improvement in speech and activity. He moves spontaneously, can dress himself though slowly and eats if food is placed before him. He answers questions rationally and clearly, shows a sense of humour but does not speak spontaneously. This improvement was maintained throughout December, and by the New Year his spontaneous activity and speech were thought to be normal.

Electroencephalogram 7.1.49: "The normal dominant rhythm of 9-a-second has increased in voltage and is now stable. The only abnormality seen is the presence of runs of 5- to 7-a-second waves in both parietal regions. The records were comparable with those before his previous discharge from hospital."

Thalamograms: Records were made from the basal structures over several hours on two occasions, while the patient was in his variable akinetic state, and again after he had recovered from it.

Summary.—A man of 39 had an acute illness associated with epilepsy and complete abolition of all spontaneous movement and all speech. There were oculomotor and vegetative signs of a lesion of the mesencephalon as well as of one in the right occipital lobe. He recovered, but the syndrome recurred in milder form a year later, when he was found to have diabetes mellitus as well as variable stupor. He again recovered. No cause for the illness was found but in view of its course, and of evidence of involvement of the cerebral hemispheres, as well as the mesencephalon, and the absence of other causes, a diagnosis of virus encephalitis involving the mesencephalon was suggested.

Simultaneous records were made of the electrical activity of the optic

thalamus, white matter and cortex of the parietal lobes, with electroencephalograms, when the patient was devoid of spontaneous movement, and when he was normal.

Experiments.—Four-point electrodes made of the end of a 22 gauge wire were introduced at a distance of 2 cm. apart into the basal grey matter, and into the supervening white matter and cortex, by means of the needle electrode which has been described and illustrated elsewhere (Williams and Parsons-Smith, 1949). Radiographs of the skull were made previously when the ventricles contained air, and later, using the same positions, with the electrodes *in situ*. In this way the radiographs could be superimposed and a composite tracing made to locate the electrodes in relation to the ventricles and inner table, and so indirectly to the grey matter of the base and surface of the cerebral hemispheres. These tracings are shown in figs. 3A and B.

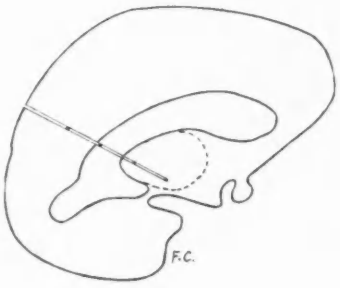

FIG. 3A.

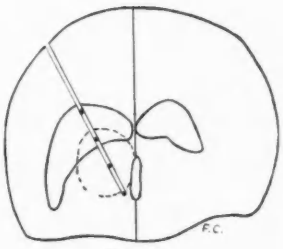

FIG. 3B.

FIG. 3.—Tracings of the ventriculograms of Case 1 with the needle *in situ*. The distal electrode is in the medial part of the thalamus close to the third ventricle. It is in the intralaminar structures of the thalamus. The second appears to be in the ventro-lateral nucleus in the posterior part of the thalamus. The proximal electrode is in the subcortical white matter, and the second is probably just in the roof of the dilated lateral ventricle. It must be remembered in interpreting these drawings that the shadow of the ventricle and the shadow of the needle do not together give an accurate indication of the relative position of electrodes to ventricle in any single picture.

It is clear that the distal two electrodes are in the thalamus. Measurements show that the distal electrode is probably in the intralaminar substance in the postero-mesial part of the thalamus. The second electrode is 2 cm. away, more lateral and posterior. The topographical studies of the ventricular shadows in relation to the structures of the basal grey matter, carried out by Talairach, Ajuriaguerra, and Hecaen (1950), have been used to locate the electrodes within the substance of the thalamus. Reference to the serial sections illustrated by these authors shows that the deepest

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electrode was in their seventh transverse section and between their first and second antero-posterior section. It may be more important to appreciate that the same kind of records, not seen in any other conditions, were obtained from the thalamus on different days, the electrodes having been reintroduced, which suggests that the discharges may not have been limited to a small area of the thalamus. As bipolar recording is used the records simply reflect the potential difference between the activity of the two contiguous point electrodes.

On each occasion the patient was lying comfortable and awake. The technique was identical with that already described. Using a six channel Grass electroencephalogram with a "bipolar" arrangement of electrodes, simultaneous records were made (*a*) from the three pairs of electrodes in the needle (*b*) from each of the electrodes within the depth of the hemispheres and a scalp electrode, and (*c*) with pairs of scalp electrodes sealed in the orthodox positions with collodion. Records were also made of the electrocardiogram. As only six recording channels were available many permutations of paired scalp electrodes had to be used. The needle made by Mr. H. B. Morton was introduced by Mr. K. Till and the radiography was undertaken by Dr. J. W. D. Bull, to all of whom we are grateful.

During the recording painful stimuli were applied, records were taken with eyes open and shut, and anæsthesia was induced by pentothal, records being made before, during and after the anæsthesia.

Records were obtained when the patient was in the state of stupor, and when he was normal.

On the first occasion (18.11.48) the patient was in an abnormal state. The experimental notes states "Is in a state of relative hypokinesis and absolute mutism lying quietly with eyes often open." As a full description of this state has already been given it is only necessary to mention that in this case and the subsequent one—a young child—the physical immobility relieved the experiment of much of its anxiety and the records of artifacts.

Results (18.11.48).—Samples of records obtained on this occasion are shown in figs. 4 to 9. They may be compared with records obtained from the thalamus of subjects with normal and with abnormal cortical rhythms (Williams and Parsons-Smith, 1949).

Electroencephalograms recorded on three occasions in four weeks during the first admission to hospital are shown in fig. 1, and on five occasions in six weeks on the second in fig. 2. The great variation in the character of the records is more easily appreciated from these excerpts than from the descriptions in the case history. The wave complexes, recurring at constant intervals (1.12.47), and present in all leads have been recognized

by us to be characteristic of a lesion in the upper mesencephalon, usually associated with encephalitis. It is probable that they occur when the lesion is diffuse and bilateral and that they are not specifically related to encephalitis. Other records were featureless except for intermittent rhythms and wave complexes which varied in form from time to time (22.11.48, 29.11.48, and 12.12.48). The patient's normal electroencephalogram showed a well-sustained and stable dominant frequency of 9-a-second of higher voltage than the most normal specimen illustrated (6.1.48). Needle electrograms were recorded on 18.11.48, 22.11.48, and 23.11.48. The features of these records are clearly shown in figs. 4 to 14, and only the pertinent details need be described here. Records from the thalamus showed bursts of waves lasting for 0.5 to 1.0 second, at intervals of 1 to

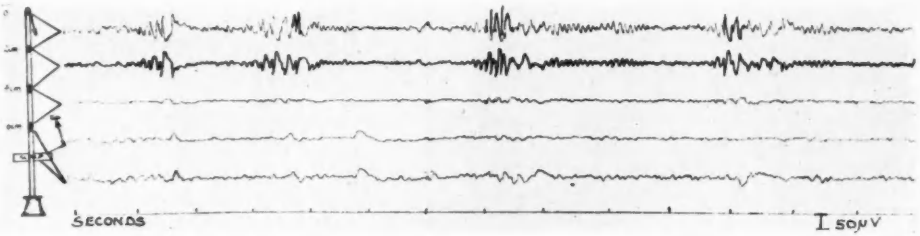

FIG. 4.—Sample of needle electrograms from Case 1 to show periodicity of thalamic discharges, with accompanying cortical disturbances while the patient was akinetic.

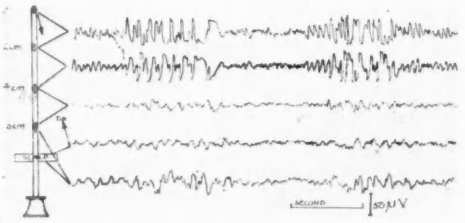

FIG. 5.—Two samples of thalamic discharges showing accompanying 6-a-second rhythms in the cortex.

5 seconds. These bursts had two main features: (*a*) rhythms averaging 12-a-second; (*b*) rhythms of 6-a-second interspersed with spikes of a higher voltage.

The 12-a-second rhythms were not composed of sine waves but of complexes made up of 12-a-second sine waves and a faster wave, possibly the first harmonic, 24-a-second. These fast rhythms usually preceded the

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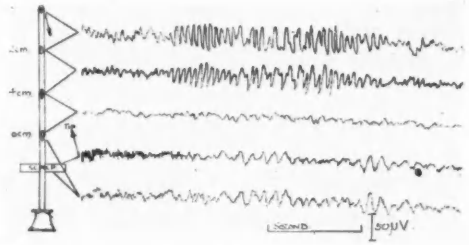

FIG. 6.—A thalamic spindle beginning with a 12-a-second rhythm which becomes coupled with a 6-a-second. The spindle is accompanied by two runs of 6- to 7-a-second waves in the cortex, which are independent of similar rhythms in the thalamus. The thalamic spindle shows a phase reversal at the second electrode.

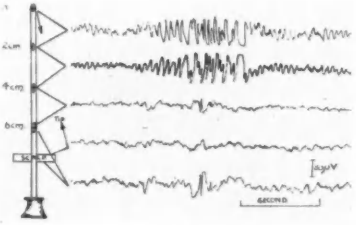

FIG. 7.

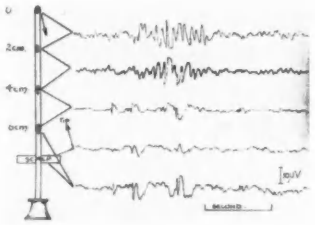

FIG. 8.

FIG. 7.—A thalamic spindle similar to that in fig. 6, showing phase reversal at the second electrode accompanied by a fast wave-and-spike in the cortex.

FIG. 8.—A short and rather poorly organized thalamic spindle accompanied by two cortical wave-and-spike complexes.

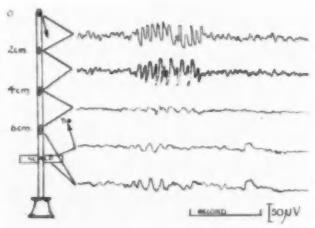

FIG. 9.

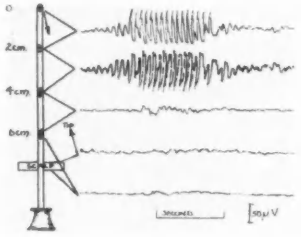

FIG. 10.

FIG. 9.—A similar spindle to that in fig. 8 showing a 6-a-second rhythm in the cortex.

FIG. 10.—Needle electrograms made under light pentothal anæsthesia. The thalamic spindle is highly organized with a 12-a-second rhythm with superimposed spikes, probably caused by fast harmonics. There is no accompanying change in the cortex.

6-a-second rhythm which followed an increase in their voltage. They continued through the period of 6-a-second activity and usually lasted beyond it. The form and duration of these outbursts varied, but their general character was stereotyped.

The origin of these rhythms could be accurately determined from the phase reversals (figs. 11 and 12) and through the process of withdrawing the electrodes 1 cm. at a time between successive recordings. They arose in the substance of the thalamus in its postero-lateral part (at the second electrode). Their spread was limited for they were not seen in the records from electrodes in the white matter overlying the ventricles, although their voltage was high with 50 to 100 μv. These disturbances in thalamic activity have not so far been recorded by us in any other condition and these thalamic records contrast strikingly with those seen in normal hemispheres (Williams and Parsons-Smith, 1949).

When these rhythmic discharges occurred in the thalamus they were usually accompanied by changes in cortical electrical activity. In fig. 4, four such discharges are seen. Each is associated with either a solitary cortical wave of 5-a-second or a short rhythm of 5 to 6-a-second sine waves. Occasionally no cortical disturbances were recorded from the surface electrodes in similar circumstances. The form of the associated cortical disturbance was not closely related to that of the thalamic discharge, and indeed it varied very greatly without any apparent relationship to any variation in the thalamic discharge. In fig. 6 two runs of 6-a-second sine waves occurred; in fig. 7 a single wave and spike complex lasting 0·25 second; in fig. 8 two similar wave and spike complexes, although the thalamic discharge was shorter in duration.

Not only was there little apparent relationship between the form of the thalamic discharge and the associated cortical discharge but the time of onset of the cortical disturbance was variable, and its duration and intensity was not proportional to that of the thalamic discharge. The important positive observation seems to be that repeated thalamic discharges occurred which had a common form. These were accompanied by cortical discharges of the kind seen during epileptic states. The thalamic discharge preceded the cortical by a variable period.

Pentothal 0·20 gramme was given intravenously once and the form of the thalamic discharge changed. It became much more stereotyped, rhythmic, clearly episodic, and frequent. It lasted longer and contained repetitive wave complexes (figs. 10 to 13). These complexes were reminiscent of the wave-and-spike discharge seen in *petit mal*, but the frequency of the complexes was 12 instead of 3-a-second. There appeared to be sine wave of 12-a-second linked with another of 36-a-second giving rise to a repeated wave complex. They lasted for 1·5–2 seconds.

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The phase reversal continued from the same point in the thalamus and the impression the records gave was that the pentothal anæsthesia had simply organized the discharges. Another change which was brought about was probably more important: although the thalamic discharges had a higher voltage, longer duration and greater rhythmicity, they ceased to initiate disturbances in the cerebral cortex during pentothal anæsthesia, whether light (figs. 10, 11, and 12), or deep (fig. 13).

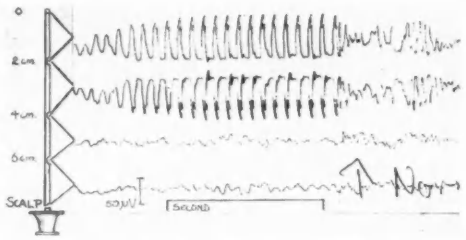

FIG. 11.—A record similar to that in fig. 10 at a faster speed. The 12-a-second rhythm of the thalamic spindle can be seen to begin before the linked fast spikes which give the wave complex its characteristic pattern. No cortical discharges occur. Notice the clear phase reversal between the two thalamic records.

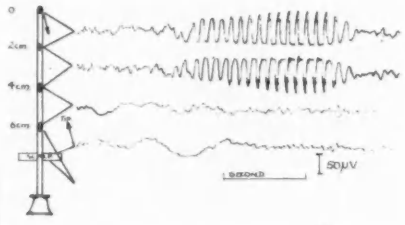

FIG. 12.—Records similar to those in fig. 11, as pentothal anæsthesia deepens. The slow cortical rhythm (about 1-a-second) stops when the thalamic spindle occurs.

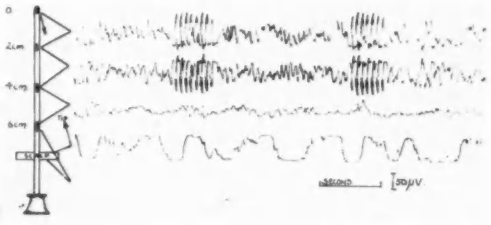

FIG. 13.—Two thalamic spindles under deep pentothal, showing the highly organized rhythmic complexes, the phase reversals and the complete independence of the cortical "coma" rhythm of 1- to 2-a-second.

The changes which have so far been described were only obtained when the patient was stuporose, but they were obtained throughout records lasting for more than an hour each, on two different days. They were not altered by pain or any other form of stimulus which we applied.

When the patient emerged from pentothal he was no longer stuporose. (Similar transient emergence after pentothal anæsthesia occurs in catatonic stupor.) He was then accessible, correctly orientated, reasonable and able to converse in an apparently normal manner, although his horizon of interest was very limited. When he had so emerged from his state of stupor the thalamic records showed no discharge of any kind. There was simply a low background of irregular fast frequencies of very low voltage, the records being similar to those of normals, at the same time the EEG records were flat and featureless as in the earlier figures (fig. 14).

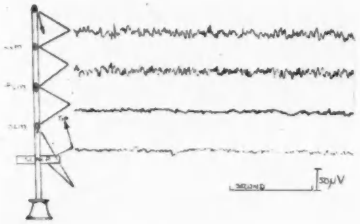

FIG. 14.—Records taken after the patient had emerged from pentothal anæsthesia. No thalamic spindles occur and the cortical records are quite flat (as in the electroencephalogram on 1.11.48, fig. 2) taken at the same stage of the illness. During this period of recording the patient had emerged from his stupor.

We have not been able to repeat the needle electrogram since the patient recovered fully, but since then his EEG has shown a normal dominant frequency of 10-a-second.

Summarizing these observations, during pentothal anæsthesia the thalamic discharges became highly organized, rhythmic and in all respects more definite. They ceased to modify the cortical electrical activity in circumstances of recording in which they had done so before. When the patient emerged from the state of akinesis and mutism and so became accessible and showed normal initiative in voluntary movement, the thalamic discharges and the associated cortical disturbances disappeared.

Case 2.—St. George's Hospital Case No. 112429.

History.—A girl aged 5 was admitted on March 4, 1949, in a variable state of stupor. She had had symptoms of upper respiratory infection for the previous two weeks. Two days before admission she started to vomit and next day became stuporose. This condition of akinesis and mutism alternated with periods of crying

and restlessness. She then had a convulsion. The day before admission the child showed oscillating movements of the eyes and twitching of the arms. She did not recognize her parents. In another hospital the child was seen to be lying on her left side with her head retracted. She resented interference. Her hands and arms were twitching. Reflexes were normal, the plantars being flexor. She was admitted to the Neurosurgical Department of St. George's Hospital under Mr. Wylie McKissock's care. There she lay quietly in bed not speaking or responding when spoken to. She did not appear to be unconscious but any rapport with her was impossible.

On examination.—Her condition was similar to that of Case 1, and need not be fully described. There were, however, frequent myoclonic twitches and shivering movements. Apart from the nervous system, no disorder was found, and there was no neck rigidity. The only disorder in the cranial nerves was the presence of spontaneous oscillating movements of both eyes, moving in a horizontal plane, with a tendency to deviate to the right.

As well as the twitching of the limbs, the tendon-jerks were brisker on the right and there were extensor plantar responses on both sides.

The following investigations were performed:

X-ray of skull: Normal.

Cerebrospinal fluid: Clear, pressure not increased, cells 22 per c.mm., lymphocytes 60 per cent, monocytes 20 per cent, polymorphs 20 per cent, protein 15 mg. per cent. Wassermann reaction negative. Lange curve: No change.

Electroencephalogram 8.3.49: Was abnormal with widespread disturbances, showing runs of high voltage 2- to 3-a-second waves, and bursts of equally high voltage 6-a-second waves (fig. 16).

Ventriculogram: The ventricles were of normal size, but there was a little bowing of the third ventricle and the septum pellucidum, which were displaced 0·3 cm. to the right.

10.3.50: The child was transferred to the Neurological Unit, with a diagnosis of acute encephalitis with involvement of the mesencephalon. She lay in stupor. There were spontaneous movements of the eyes, disturbed by irregular oscillations. There were occasional clonic shivering movements of the jaw with irregular myoclonic twitches in the arms, especially the left. These could be evoked by painful stimulation. No new neurological signs were found.

12.3.49: She began to improve. The myoclonus was less frequent, the oscillatory movements of the eyes less evident. Attacks could still be induced by stimulation.

10.3.49: She was more alert and would obey commands and would open her mouth when told to do so. She lay still in bed, but when a sensory stimulus of any kind was used, violent myoclonic jerks occurred in all limbs.

20.3.49: She recognized people, fed herself and was continent. She continued to have attacks on sensory stimulation, and these were now associated with aggressive behaviour and outbursts of rage. She continued to improve and was discharged on 14.4.49. Repeated electroencephalograms were recorded and samples are shown in fig. 16.

Experiments.—A needle electrogram of the thalamus was recorded on 8.3.49; twenty-four hours after the ventriculogram, when the girl was in stupor, complicated by myoclonic jerks in response to stimulation. Radiographs of the needle *in situ* showed the tip to be 1 cm. from the mid-line, 4 cm. above and 1 cm. behind the posterior clinoid process (fig. 15).

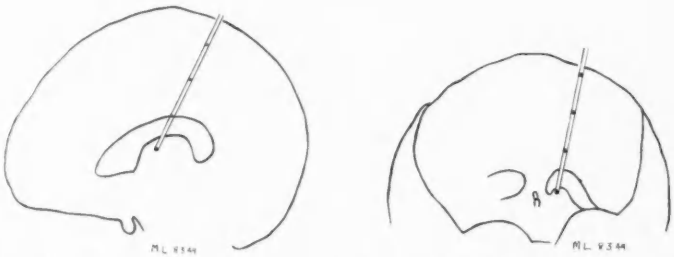

FIG. 15.—Line drawings of the ventriculograms with superimposed needle shadow in Case 2.

Electroencephalogram 11.3.49 shows continuous abnormality. Records from the frontal lobe show rhythmic 3-a-second waves with high voltage, interrupted by spikes. Other records show irregular 1- to 3-a-second waves with occasional runs of high voltage 6-a-second waves.

Needle electrogram 11.3.49: This showed many abnormal features depending on the child's state at the time of recording.

(1) The high voltage rhythmic waves seen in the electroencephalogram were seen, by phase reversal (fig. 17), to be arising deep in the hemispheres.

(2) During an attack, whilst akinetic, rhythmic 8-a-second waves having a high voltage, occurred in bursts in the thalamus. These were associated with rhythmic 2-a-second waves in the cortex.

Electroencephalogram 4.4.49 (fig. 16): On recovery showed an

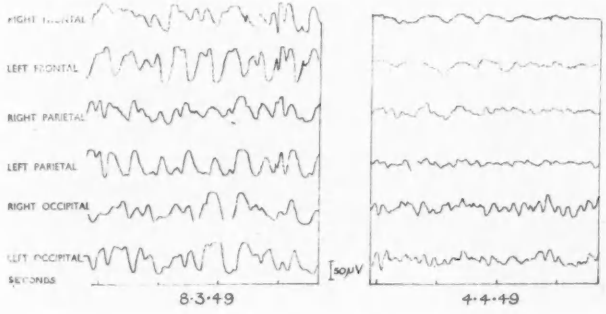

FIG. 16.—Electroencephalograms recorded on Case 2 during the period of stupor and on recovery.

unstable dominant frequency ranging from 7- to 9-a-second, with a normal distribution. There were occasionally also runs of rhythmic 3- and 4-a-

second sine waves having the appearance of small epileptic discharges. These were seen equally well in both frontal lobes.

Needle electrogram, 4.4.49, was in great contrast to that made nearly a month before (cf. fig. 17 with fig. 18). Now direct corticograms showed

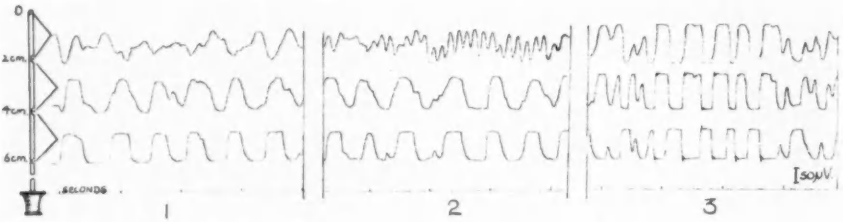

FIG. 17.—Needle electrographic recordings from electrodes in the positions seen in fig. 15, made while the patient was in stupor, having frequent tonic fits. 1, Rhythmic waves of 2-a-second arising subcortically with a phase reversal between the top two records, having a pure wave form in the cortex. 2, A rhythm of 8-a-second arising in the thalamus, independent of the 2-a-second rhythm, which continues uninterrupted (cf. fig. 13). 3, A burst of very high voltage waves of 2-a-second coinciding with an epileptic attack. The phase reversal of the waves is more superficial than in 1 and 2.

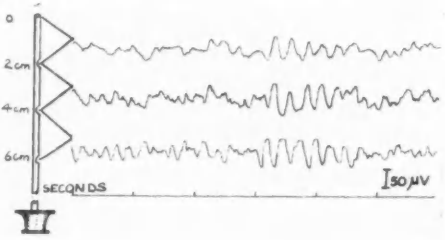

FIG. 18.—Needle electrographic recordings during recovery from the encephalitis with akinetic mutism. The conditions of recording are similar to those in fig. 17. The only thalamic activity seen is a reflection of a spindle of 4-a-second waves with a phase reversal in the lower two records, indicating a subcortical origin. The records are much more normal than those in fig. 17.

rhythms similar to the electroencephalogram (fig. 16). The records from the thalamus showed little organized activity recognizable as distinct from that of the cortex. On the contrary the only rhythms seen in thalamic records were reflections of 4-a-second rhythms arising within the cortex (fig. 18).

Summary.—A girl of 5 was admitted to hospital in a state of stupor with myoclonic epilepsy in response to stimulation. During the stupor rhythms of 8-a-second arising in the thalamus were associated with 3-a-second rhythms in the cortex. When the state of stupor ended and normal behaviour appeared, the rhythmic thalamic activity disappeared.

Discussion

Akinesis with mutism has been described in a number of instances of organic disease of the nervous system, notably when structures near the third ventricle have been damaged by tumour. Electroencephalographic changes in such cases as these have been described by Walter, Griffiths and Nevin (1939) and by Cairns *et al.* (1941). The changes they described in the electroencephalographic records were similar to those seen in the present 2 cases.

In these present cases, however, records made from the structures near the third ventricles at the same time as others from the scalp, cortex, and white matter offer new information upon the subject. The disturbances which have been described may be related to coincident experimental work in animals, which concerns mainly the relationship of the intralaminar substance of the thalamus to the activity of the cerebral cortex. It may also be used in the study of the mechanisms of consciousness and movement.

The site of origin of the thalamic rhythms.—The contemporary important work on thalamo-cortical reactions, initiated by Morison and Dempsey (1942) and reviewed by Rose and Woolsey (1949) and Jasper (1949) makes it clear that the origin of electrical changes within the thalamus must be precisely known, at least to the limits of the nucleus responsible, if their meaning is to be understood. A stereotactic machine for the placing of electrodes in the human thalamus was described by Talairach, Hecaen, David, Monnier, and Ajuriaguerra in 1949, and others have been built by Hayne, Belinson and Gibbs (1949) and Spiegel and Wyciss (1950). It may be that the lack of uniformity in the records we have made from the thalamus (Williams and Parsons-Smith, 1949) is due in part to the differences in the resting electrical activity in the different thalamic nuclei. In these cases we have therefore related the topographical charts prepared by Talairach, Ajuriaguerra and Hecaen (1950) to the radiological studies of these cases, to localize the position of the electrodes in the thalamus.

This process showed that in the first case the recording electrodes were in the posterior part of the thalamus. The distal electrode was in each in the medial part, in the intralaminar structures. The next electrode was 2 cm. more posterior and lateral, and was in or near the postero-lateral nucleus. It was from this second electrode that the remarkable rhythms seen in Case 1 arose.

The type of thalamic discharge.—Although the patients were continuously in stupor during one period of recording, the thalamic discharges and their associated cortical disturbances were episodic. They consisted

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of spindles of 6- and 12-a-second rhythms, with intervals of quietness between them. Very similar bursts of spindles of activity were found in the thalamus of anæsthetized cats by Dempsey and Morison (1942). They were recorded in unanæsthetized cats with partial bilateral mesencephalic section by Lindsley, Bowden, and Magoun (1949). There is a very close similarity between most of the characteristics of the spindles seen in Case 1 and in the experimental animals. The frequency (12-a-second), the faster rhythms associated with this rhythm, the shape, duration and periodicity of the spindle were all similar (*see* fig. 6 of their paper). Furthermore the relationship of cerebral rhythms to their thalamic spindles was similar to that in our case (*vide infra*). It is also significant that the sites in the cat's thalamus from which they recorded the spindles (fig. 7 of their paper) coincided with the site of origin of the spindles in our case, i.e. the postero-lateral nucleus and its neighbourhood. In Dempsey and Morison's (1942) cats, barbiturate anæsthesia was present; in Lindsley, Bowden and Magoun's the reticular system had been cut; and in our patients the mid-brain was involved in an inflammatory process.

The whole question of the occurrence of spindles or bursts of rhythmic activity, in the cortex and thalamus of animals under anæsthesia, with decortications, and with brain-stem sections is discussed by Lindsley, Bowden and Magoun, so that it need not be reconsidered here. This tendency to spindling has been recognized in the electroencephalogram in states of relaxation or sleep. It has been described by Bremer (1936 and 1937), and Lindsley, Bowden and Magoun found that mesencephalic or diencephalic section, *so long as it involved the ascending reticular activating system*, produced spindling which was like that of normal sleep or barbiturate anæsthesia. Although the authors point to the clinical observation of somnolence in mid-brain lesions in man, and although they carefully consider all the evidence and theories available, they observe that the nature of the spindles is thoroughly obscure. "It is disconcerting to realize that this feature of the electroencephalogram which in the amount of study devoted to it, is probably second to the alpha wave, with which its frequency is identical, is like it also in being still so little understood."

The frequency of the rhythms within the spindles was 8-a-second in one of our cases and 12-a-second in the other, within the frequency range of the alpha rhythm, but there is no doubt that these rhythms arose in the postero-lateral part of the thalamus, and that they were not associated with similar rhythms in the cortex. Lastly the thalamic spindling was only seen during the phases of stupor, when scores of examples were recorded

within about an hour's recording, while none were recorded in a similar period in either case after recording in a normal state.

Whereas pentothal organized the rhythmic activity within the spindles, presumably by abolition of frequencies other than the primary rhythm in the spindle and its harmonics, as well as by potentiation of those rhythms, recovery from pentothal also provided the means of emergence from the stupor with abolition of the spindles.

Relationship of thalamic to cortical activity.—The spindles of rhythmic discharge in the thalamus were associated with disturbances in the electroencephalogram and electrocorticogram. These disturbances in the cortex were less marked than those in the thalamus, they were shorter in duration and they usually started later. Although the pattern of the thalamic discharge was constant, the cortical discharges were variable as the figures show. They included irregular waves of different frequencies, rhythms of 6-a-second and isolated waves and spikes (Figs. 6, 7 and 8). Furthermore the cortical discharges were not a direct reflection of the thalamic. This supports our earlier observations, for although identical epileptic discharges have been recorded from the basal grey matter and the cortex, it is our view that direct electrical spread of discharges recorded simultaneously in different parts of the brain may lead to confusion as to their physiological significance. From the illustrations and descriptions presented in this paper, it seems that the rhythmic discharge arising in the thalamus is primary and the less organized cortical disturbance which starts later is secondary to it. The cortical responses to the thalamic discharge are various, but most of them are reminiscent of so-called "larval" epileptic disturbances. They were generalized and bilateral. The delay in the cortex is similar to the recruitment response described by Morison and Dempsey.

Although cortical spindles of rhythmic activity are well recognized in barbiturate anæsthesia in animals and man, and although pentothal anæsthesia accentuated the rhythms within the spindles recorded from the thalamus in our case it abolished completely the cortical rhythms which had been associated with them in the unanæsthetized stuporose state.

Moruzzi and Magoun (1949) in their studies on cats, found similarly that under barbiturate anæsthesia bulbo-reticular stimulation was much less effective in activating the E.E.G. than in unanæsthetized preparations. It is impossibde to select any one explanation for this. As Bishop (1949) says: "with all the evidence of demonstrable or possible interaction between thalamus and cortex, there are also signs of capacity for independent action where inter-connexions are severed." Although no explanation

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can be offered it must matter that the cessation of the cortical "response" to the thalamic discharges which was brought about by pentothal was followed by emergence from the stupor and cessation of the thalamic discharges—evidence surely that cortex and thalamus were responsible together for continuing the abnormal state.

Relation of the thalamic discharges to the state of stupor.— As we were able in 2 patients to record thalamic discharges which were not present on recovery, and which in Case 1 disappeared on remission after pentothal, the discharges can be directly related to the mental state. Since similar disturbances had not been seen in a number of cases of symptomatic and idiopathic epilepsy, they can be related to the stupor as such. A number of instances have been quoted in which animal experiment has led to similar thalamic activity. The most important is section of the reticular activating substance in the mesencephalon. Following the work of Dempsey and Morison (1942) evidence accumulated, which has recently been summarized by Jasper (1949), which indicated that the intralaminar substance of the thalamus has widespread effects on the activity of the cerebral cortex.

It seems to be a lesion of this integrating or activating mechanism which in animals causes spindles both in the thalamus and in the cortex similar to the thalamic discharges seen in these 2 cases.

It is important to keep a clear distinction between somnolence and stupor, for akinesis can occur without sleep. In our patients there was absence of movement and in this connexion Moruzzi and Magoun (1949) found that when the brain-stem reticular formation in cats was stimulated, although afferent volleys arrived at the cortex, the muscular contractions expected under the chloralose anæsthesia they were using were abolished. At the same time, however, spinal reflex activity was preserved. Bishop (1949) has speculated that the spontaneous rhythms recorded from the central nervous system are complementary to the induced potential changes caused by functional activity of the nervous system, and he wonders whether in some way they modify the background for this functional activity. Stimulation of the reticular substance in the mesencephalon causes inhibition of spontaneous and induced rhythms both in the cortex and thalamus (Moruzzi and Magoun, 1949) and this inhibition is unilateral if one side is stimulated. On the other hand interruption of the reticular substance gives rise to the spindles in thalamus and cortex similar to those we have described. In animals the first state is associated with wakefulness and the second with somnolence. In man also, as far as the E.E.G. is concerned, wakefulness is associated with disappearance of spontaneous rhythms, and sleep or anæsthesia with spindling. It seems as if in

man, too, spindles of rhythmic activity in the thalamus are associated with cessation of cerebral activity. All this evidence may be related to clinical knowledge of cases of akinesis with mutism. The causal lesions are in or near the third ventricle and now we see that there is disturbance of function in the thalamus which produces secondary changes throughout the hemispheres. From indirect evidence the causal lesion is in the brain-stem reticular system, which is an inter-relating system concerned with ascending pathways and which is thought to activate and integrate the whole afferent system, so that impulses are modified by it before passing through the thalamus for integration into behaviour in the cerebral hemispheres. If this proves to be the case, stupor in these cases may be due to a disturbance of the integration of afferent impulses, resulting in effect in a cerebrum isolated from its environment.

SUMMARY

(1) Thalamic electrograms were recorded in 2 patients who had clinical signs of a mesencephalic lesion. Records were made when they were akinetic, and mute, and on recovery.

(2) Spindles of electrical rhythms were recorded from the postero-lateral region of the thalamus during stupor only.

(3) These episodic discharges, which have not been recorded from the human thalamus in other conditions including coma, were associated with episodic waves in the cerebral cortex.

(4) Spindles were more frequent and their rhythmic character more evident under pentothal anæsthesia, but this abolished the associated cerebral cortical disturbances.

(5) Similar changes have been found by other workers in the thalamus and cortex of cats in which the reticular substance of the mesencephalon has been divided.

(6) The present observations have been related to the results of animal experiment and to the present knowledge of thalamo-cortical mechanisms.

(7) On the basis of this work it is suggested that in akinesis with mutism (stupor), the inactivity results from disturbances in the ascending reticular system, which is concerned in the integration and activation of afferent impulses.

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SOME CLINICAL ASPECTS OF HUMAN CORTICAL FUNCTION

BY

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"What right have we to conjoin mental experience with physiological? No scientific right; only the right of what Keats, with that superlative Shakespearian gift of his, dubbed 'busy common sense.' The right which practical life, naïve and shrewd, often exercises."

Sir Charles Sherrington, "The Brain and its Mechanism." Rede Lecture, Cambridge, 1933.

ORGANIC disease of that part of the human cerebral cortex which lies posterior to the central fissure of Rolando gives rise to a variety of specific disturbances of function which, in so far as they impair an individual's cognitive behaviour, might be called disorders of consciousness. These disorders are mainly concerned with vision and hearing, with the sensations of touch, pain, vibration and posture, with stereognostic sense and tactile discrimination, with language in all its aspects, the faculty of calculation, voluntary movement, and awareness of the body and its orientation in space.

Disorders of this nature have long been recognized and have been discussed by various authors since the middle of the last century. They were originally separately described as if each belonged to a specific category of dysfunction—as dysphasia, dyslexia, dysgraphia, dyspraxia, dyscalculia and so on—although a single disorder is rarely seen without accompanying allied disturbances.

This separation into categories has led to the assumption that each dysfunction is an isolated morbid entity, which hypothesis has lent support to those authors who hold that "centres" exist in preordained, well-defined areas in the cortex (and, more particularly, in the case of the functions in question, in the "parietal lobe") which control speech, writing, reading, spelling, calculation and other faculties.

An opposite view is held by other authors, who argue against such precise anatomical localization of function.

At present, no satisfactory theory exists which defines the processes of disintegration which affect cognitive behaviour.

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This paper discusses the results obtained from the intensive examination of a series of patients suffering from organic disease of the brain which caused defective cortical function of the nature described above.

The following functions were disturbed:

(i) *Language*, which, broadly defined, includes expression and comprehension of spoken and written speech and mathematical symbols, gesture, music and song.

(ii) *Calculation*, which also involves language and the use of mathematical symbols.

(iii) *Voluntary Movement*, including the ideational and motor performance of writing, drawing, and construction in planes of two and three dimensions.

(iv) *Orientation of the body in space and time*, which involves the conception of the body-image.

(v) *Colour gnosis*.

(vi) *Memory*.

These functions will later be analysed in greater detail. It will be shown that no single function is an isolated performance. Each depends upon the organization and synthesis of many functions. They all depend also upon that ill-defined factor called "intelligence," and upon the previous education and the environment of the individual.

The conclusions reached at the end of the examination of the clinical material led to the formulation of the following hypothesis:

The cerebral functions mentioned above are all dependent upon perception, and the disorders of function are themselves disorders of some aspect of the processes which lead to perception.

Perception will here be defined as a phenomenon which is the qualitative experience of a conscious individual, and which is evoked by a series of events, including the unconscious reception, selection, differentiation, integration and interpretation of sensory stimuli.

According to this hypothesis, a basis for the classification of the disorders of function mentioned earlier will be suggested. The hypothesis will be further developed and its application demonstrated in the following pages.

Perception

A sensory stimulus may evoke a sensory perception. Sensory perception is here defined, as has been stated previously, as the qualitative experience of a conscious individual, which occurs as the result of the unconscious reception, differentiation and interpretation of a sensory stimulus. It may be assumed that the faculty of perception is an inherent property of mind.

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We have little knowledge of the precise nature of sensory stimuli and the differences between them before they are perceived, but once perceived they evoke sensations of well-defined qualities. These may be broadly described as belonging to the categories of hearing, vision, taste, smell and "feeling," which includes the senses of touch, pain, temperature, posture and vibration. While the finer interpretation of sensory stimuli depends upon experience, even newly born children are capable of differentiating crude stimuli. The perception of stimuli is accompanied by affective states appropriate to the quality of the perception—such as fear, with a painful stimulus, happiness, with a pleasant one. At a very early age in life, stimuli are yet further differentiated. For instance, touch stimuli may be painful or pleasurable; visual stimuli may be recognized as being dim or bright. In young children the faculty for the differentiation of sensory stimuli develops rapidly, so that dimensions are gradually perceived, sounds are known to be voice sounds, or sounds made by particular objects—for example the clock, the piano, and so on, taste develops, so that finer gradations of sweetness or sourness are appreciated, and touch brings awareness of texture and shape of objects.

When a specific sensory stimulus evoking a perception has been repeated, possibly more than once, an image or memory of the experience may be formed and learned, which embodies the characteristics and quality of the sensory perception, together with its affective accompaniment. This image may belong to any sensory category. It may be visual, auditory, gustatory, olfactory, and so on. It may also be kinæsthetic or kinetic. That is to say, voluntary movement is perceived qualitatively, as a synthesized pattern of activity. It is not perceived in its component physiological parts as the isolated actions of muscles, combined with postural sensibility and so on. Kinetic images, therefore, are memories of integrated, purposeful movements.

Multiple memory images may be formed of succeeding like perceptions. The latter can never be precisely similar, because the environment, the affective states, the quantity of stimuli, inevitably change from moment to moment in time. Perceptions are, in addition, the products of previous experiences, each one depending upon the sum of its predecessors.

Another inherent property of mind now influences development, which may be defined as the faculty of abstraction. When a number of memory images have been formed, it is possible for an individual to abstract from them their common qualities. The sum of these qualities may be represented by a symbol. Symbols may take forms common to all mankind, and presumably determined by evolution, or forms determined by the civilization and culture of the particular community (for example, its language, its songs, its customs), or they may be of a pattern

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of peculiar significance to a single individual. Whether the symbol is of formal nature or not, the perception which it evokes retains, at this stage, a connexion with its origin, the images, which were derived from personal qualitative experience. While the events which evoke sensory perceptions are never exactly alike, the symbols include all the characteristics and qualities of all the perceptions and images previously experienced in the particular category of that stimulus. The symbol thus represents compound experience in a condensed form.

Abstraction may proceed. The symbol may now be entirely detached from the state of immediate sensory perception, and exist as an integrated complex. (An example of this is the conception of a generic noun.) Once this has occurred, a succeeding sensory stimulus of a certain order, or the perception of the symbol belonging to that order, will bring into consciousness the complete compound experience of that order, namely, all previous images of perception and their accompanying affects.

After early infancy, then, single or isolated perception of sensory stimuli scarcely occurs. Each perception is a complex of inextricably entangled previous perceptions.

We therefore approach all succeeding sensory perceptions with highly organized prediction. For example, we see a white object upon a distant table. At once we are aware of a vast order of memory images and predetermined expectations. The white object may be a cup, a plate, sugar, a handkerchief, a piece of bread. Immediately we recognize the object clearly, we find our visual perception of it inevitably adherent to perceptions of another order, concerning its texture, weight, taste, smell and so on, images which are associated with handling or eating the object. The more familiar we are with the object and the greater the extent of our experience regarding it, the wider will be the range of our expectations and images. We will also include in our perceptions all the information we have gained regarding the object from the instruction of our parents and teachers, books, the radio, and so on.

The immediate sensory perception of the object, its visual quality, now recedes in importance. We have taken for granted what we assume to be its concrete existence, its characteristics and qualities. The symbol, which for us embodies the whole complex of sensation which we associate with the object, may, following detachment from the immediate sensory perception, persist while the latter ceases.

We may thus imagine a state of affairs in the brain in which a system of perception images is formed together with affective associations. We may assume also the existence of a system of symbolic complexes representing groups of memory images.

A further development may take place. The symbols may be abstracted

from their position in regard to memory images, and receive, as it were, an individual existence. They become highly elaborated and far removed from the original sensory perceptions. The science of mathematics is such an elaboration of abstractions. That such systems of abstractions are essentially derived from sensory perceptions, however remotely, is a fact which is often forgotten.

Every succeeding sensory perception is, then, to the individual throughout life, the sum of all previous experiences of related perceptions with the addition of the present one.

The practical implications of the hypothetical sequence of sensory stimulus → sensory perception and affective state → memory image → symbolic representation → abstraction, are to be seen in regard to language, and disturbances of language in organic brain disease, in the following example:

The word "sugar" represents to English-speaking people a very elaborate structure of images. If we hear this word, we are immediately aware of all its qualities and characteristics simultaneously. It is sweet, white or brown, granular or lump, crystalline, rough, odourless, sticky when wet, crunches between the teeth, and gives us a peculiar sensation and sound when we tread on it. We have, then, a compact bundle of associations of visual, tactile, auditory, gustatory and olfactory nature. The complexity of our associations depends of course upon our previous experiences, but ordinarily, to every English-speaking person who has a normal sensory system, the word "sugar" conveys all the images mentioned, and we are aware of them the instant we see the concrete substance sugar, or hear, or say, the word "sugar." Furthermore, we have learned the shape of the symbols which form the written word, and when writing or reading the word, we are also aware of its sound when spoken. The words, whether spoken or written or read, are symbolic representations of the concrete substance, and both the former and the latter may arouse in us the conscious perception of their whole complex of associations. We know also, without personal experience, that is, in abstract form, that sugar may come from cane or beet, that these plants grow in hot or temperate climates in different parts of the world. We are aware, too, of a thousand ramifying associations, which also occur spontaneously, such as tea, cake, shortage, ration, and so on. "Sugar" will, in addition, bear a great variety of affective accompaniments for every one of us. The final perception of "sugar," however, while having presumably a like significance for two or more individuals of a particular community (for otherwise we could not communicate with one another by means of language), must differ considerably in its more subtle aspects from man to man. Our perceptions are the sum of our highly organized, highly individual experiences.

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An organic lesion of the brain may affect the perception of "sugar" in a number of ways:

(1) At the highest level of cortical function the existing system of abstractions and the ability to perform abstractions will be affected. A patient may thus be no longer able to understand or to remember the details of abstract associations—the significance of the ration, the world shortage and so on (Goldstein, 1939, 1948).

(2) At another level, symbolic representations may be affected. The word "sugar," either in spoken or written form, may be without meaning for a patient. If the symbols alone are destroyed, the patient may still be aware of the complex of associations and images aroused by a stimulus, but he will be unable to express these, or understand them in symbolic form.

(3) The memory images themselves may be destroyed by disease. Thus while a patient is able to perceive the white crystals of sugar, he is in the position of one who experiences such sensations for the first time and cannot relate them to previous experience. He therefore does not recognize the substance "sugar." He may never be able to retain images again, so that each separate sensory perception is new, pertaining to the particular concrete situation. The symbolic forms are of course meaningless to such a patient.

(4) Sensory perception itself may be faulty—that is, there may be an interference at the juncture where the sensory stimulus becomes perceived. The patient is unable to perceive correctly the colour, or texture, or taste of sugar, or the sound of the word "sugar." While previous images and symbols still exist, the stimulus cannot be associated with them, and the resulting imperfect sensory perception is meaningless to the patient, as occurs in visual or auditory agnosia.

(5) Finally, at a peripheral level, the receptors of sensory stimuli, as the eyes, or ears, or tongue, may be affected by disease, and the stimuli may be unable to reach the cerebral cortex.

This hypothesis, that certain cortical functions are dependent upon perception, and that disturbance of such functions is due to a defect of the process of perception, will here receive a clinical application.

Description and Analysis of Language, Calculation, Voluntary Movement, the Orientation of the Body in Space and Time, Colour Gnosis and Memory

I. Language.

Defective function of language has been described since the days of Gall (1807), Bouillaud (1825), Lordat (1843), and Dax (1865). The term

"aphasia" was originally used by Trousseau in 1864, although three years earlier Broca had published some cases of "aphemia" or loss of speech, as the result of cerebral destruction, which he demonstrated at autopsy. Broca was one of the first to adopt the theory that speech is controlled by a well-defined cortical "centre," which he localized at the base of the third frontal convolution. In 1864 Hughlings Jackson developed the psychological, or functional, approach to the problem of language. He was later supported by Pick (1909), Marie (1906 and 1917), Head (1926), Goldstein (1927), and others.

In opposition to this view were those who adhered to the doctrines of cerebral localization, following the teaching of Broca, and such authors included Bastian (1898), Wernicke of Breslau (1874), who originally described "sensory aphasia," Henschen (1920 and 1925), Kleist (1934), and many others.

Today opinion is still divided as to whether language is controlled by a localized centre in the cortex, or whether it is, as Jackson (1864) believed, "a function of the whole brain. Speech cannot be located in any small area of the brain. It must require a vast representation." Language will be here defined (as has been mentioned above), as including the comprehension and expression of spoken speech, written speech, and mathematical symbols, gesture, music and song.

(i) *Comprehension and expression of spoken speech.*—These functions depend upon intact organs for the reception and perception of sound, upon the ability to integrate and use previously learned symbols of an acoustic and kinetic nature, and upon intact organs for the production of sound. In order to express sound symbols (i.e. words and sentences) intelligible to others, the individual must also have the ability to organize "thought"—that is, he must be aware of what he wishes to say. Thinking is partly dependent upon pre-existing symbolic images. Abstract thinking is entirely dependent upon them. Thinking also depends upon the ability to abstract, and upon the ability to sort, or classify, perceptions. Expression of speech involves the use of grammar, and, as with music, the rhythm, fluency, cadence and emphasis are important factors.

(ii) *Comprehension and expression of written speech, that is reading and writing.*—(*a*) *Reading*: Silent reading is dependent upon intact vision (except in the cases of specially educated blind persons), upon correct visual orientation, and orientation of the self in two-dimensional space, upon the ability to spell and the ability to integrate and associate previously learned visual symbols in the form of letters, words and punctuation marks. Knowledge of grammar is also necessary. In order that the material read should have meaning for the individual, he must be able to recall what he has read in previous sentences or paragraphs. (Reading aloud is possible

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without recognition of meaning, even though silent reading may be meaningful.) The faculty for remembering what has been read may be described as the ability to retain visual perceptions in the form of meaningful images.

Reading aloud is dependent upon all the above factors, and also upon the factors essential for speaking aloud.

Defects of reading have been grouped under the general term *dyslexia* and have been frequently described in the literature Broadbent (1872), Kussmaul (1885), Goldstein (1910), and Henschen (1925).

(*b*) *Writing*: This function is dependent upon all the factors mentioned as necessary for the functions of reading and speaking, and, in addition, upon kinetic images and symbols which are concerned with the performance of voluntary movement (praxis). Constructional apraxia may be the essential factor in certain defects of writing.

Defects of writing have been grouped under the term *dysgraphia* (Ogle, 1867; Charcot, 1883; Dejerine, 1885; Pötzl, 1928).

(*c*) *Music and Song* also depend upon a specific system of symbols, but, in addition, require a sense of *rhythm*, tone and pitch. They also depend upon all the factors mentioned above as being necessary for the functions of speaking and writing speech.

Singing, however, may be, at times, an automatic performance.

Defects in the understanding or the performance of music are grouped under the term *amusia* (Henschen, 1920; Teufer, 1924; Goldstein, 1927; Feuchtwanger, 1930).

(*d*) *Gesture*: Gesture may be automatic, as a shrug of the shoulders, or may be in the form of deliberate mime. Automatic mimetic movements may best be termed *gesticulation*. Deliberate mime, or *pantomime*, is a performance which aims at expressing an idea. Both gesticulation and pantomime may be used for the purpose of emphasizing speech, or as a substitute for speech. Certain races are more apt to employ gesture than others. The Latins, for example, use gesture more freely and readily than the Nordic peoples. This is probably due to their traditions and culture rather than to inherent racial characteristics. Pantomime may be sufficiently expressive to enable strangers to communicate with one another, who have no knowledge whatever of each other's languages.

Gesture may be stylized, and follow strict conventions, as in the Deaf and Dumb sign language, or it may have a very precise symbolism as in oriental dancing.

Both spontaneous automatic gesticulation and pantomime may be affected by organic disease of the brain. Patients suffering from aphasia may have a relative poverty of gesture. Apraxia may prevent the per-

formance of pantomime. In rare cases of jargon aphasia, gesture may be exaggerated (Critchley, 1939; Goldstein, 1948).

It must be emphasized that the mechanical division here of language into categories of function does not intend to imply that language consists of many separate functions. It may be said rather to be the synthesis of multiple complex aspects of a single function.

Not all aspects are covered by this classification. Certain indefinable qualities belong essentially to language, including the sense of poetry, of religion, of humour, of race and culture, endeavour and creation.

II. Calculation.

The use of *Mathematical Symbols* involves all the factors mentioned above for the speaking, and writing, and reading of words but the essential symbolic images are in the form of figures, specific signs as $+$, $\times$, $-$, $\div$, and specific geometrical designs and algebraic formulæ.

Calculation itself is probably a particular faculty apart from the mere ability to understand and use the symbols involved. Mathematical symbols are of a very abstract nature. Defects of calculation are grouped under the term *dyscalculia*. The varieties of dyscalculia are as diverse as the varieties of dysphasia or amusia.

III. Voluntary Movement.

Voluntary movement is partly dependent upon (1) the perception of superficial and deep sensation, and (2) motor power and co-ordination.

In order that movement may be performed at will, therefore, there must be the ability to organize and integrate images and symbolic patterns of kinæsthetic and kinetic nature. Voluntary movement also depends upon intact orientation in space in two or three dimensional planes, and upon the will to perform a purposeful movement.

Disorders of voluntary movement have been grouped under the term *apraxia*. Many classifications of apraxia have been suggested, none wholly satisfactory (Liepmann, 1900; Heilbronner, 1910; Goldstein, 1927; Sittig, 1931; Kleist, 1934; Gooddy, 1949). Kleist described a specific type of apraxia which may exist as an isolated entity. This he termed *constructional apraxia*.

IV. Orientation in Space.

Correct orientation of the body in space depends upon the following:

(*a*) *The knowledge and understanding of the relationship of the parts of the body of the individual to the whole*—that is to say, the proper orientation of the internal environment of the self. This is related to the conception of the *body-image*, which has been defined by Critchley (1949) as the "mental idea which an individual possesses as to his own body and its physical and æsthetic attributes." The conception of the body-image

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has been described by Head and Holmes (1911 and 1912), Schilder (1935), Lhermitte (1939), and others.

Defective conception of orientation within the self is seen when organic cortical lesions give rise to the symptoms of "right and left disorientation," finger agnosia, or agnosia for different parts of the body (autotopagnosia), or neglect or unawareness of one or other side or a portion of the body, as is sometimes the case in hemiplegia.

The body-image depends of course on an intact sensory system—that is, an intact system of sensory images and symbols. Such phenomena as tactile or visual inattention may perhaps be disorders of the body-image due to impairment of sensory perception, sensory images, or sensory symbols (Bender, 1945; Critchley, 1949).

(*b*) *Relation of the self to the external environment.*—Time is relevant in this connexion, as orientation may be defective either regarding previous experience (that is, past time) or regarding immediate environment (present time).

Defective orientation in past time implies that an individual is unable to recall previously learned topographical data—for example, concerning his house, street, town and so on. He is unable to orientate himself correctly in regard to past situations. This is a defect of previously experienced perceptions now existing in the form of images. Defective orientation in present time implies that an individual cannot learn to find his way about in unfamiliar surroundings, however long he remains among them; for example, a patient who is never able to recognize his own bed in hospital (Goldstein, 1928). This is a defect of sensory perception. The individual is unable to form memory images of his surroundings because he perceives in a faulty manner, and objects appear unfamiliar.

(*c*) *Relation of objects in the external environment to one another in two and three dimensional planes.*—Visual disorientation may play a large part in disorders connected with disorientation in the external environment. Visual perseveration, and poor visual acuity with hallucinations, may also be a cause of such disorientation.

Nevertheless, patients with moderately good vision may be disorientated regarding objects in their surroundings. The difficulty may be one concerned with the faculty of abstraction. The patient may be unable to comprehend the meaning of such terms as nearest, farthest, north, south, beyond, and so on, although his speech is not otherwise affected. Such a patient may be incapable of judging distance and quantity, relative heights, depth, and the differences between geometrical shapes.

Cases of patients who suffered from disorientation of the body in space have been described in the past by many authors—Pick (1922), Minkowski (1923), Gerstmann (1924 and 1932).

V. Orientation Time.

Correct orientation in time depends also upon the relation of the individual to his environment, but in this case the latter is temporal, not spatial.

In organic lesions, defective orientation in time is generally accompanied by defective spatial orientation. In psychoses, temporal disorientation may occur alone, and is especially seen in schizophrenia.

Patients suffering from disorientation in time may be quite unable to judge the passage of time correctly. Their sense of time may be altered so that time seems to them to pass more slowly or more quickly than is normal to them. They may be confused as regards the correct orientation and sequence of events in the past. They may have the sense of familiarity or previous experience (the sense of "déjà vu") where none should exist.

Altered time sense has been described by Lewis (1931).

VI. Recognition of Colours.

Recognition of colours in a person not congenitally "colour blind" seems to depend upon a special faculty, and the defect thereof is unrelated to "colour blindness." Colour agnosia may occur in a patient who has moderately good vision, and who has no nominal dysphasia. It is essentially a disorder of the recognition of colours. It may accompany dyslexia.

Colour agnosia has been described by Lewandowsky (1908), Sittig (1921) and others.

Goldstein and Gelb (1924) have described a case in which there was difficulty in naming colours in the abstract, possibly due to a specific dysphasia.

VII. Memory.

Memory is dependent upon sensory perceptions, images of perceptions, symbolic images, and the ability to organize and integrate these images. That is to say, it is not a specific function. Hughlings Jackson laid stress on the importance of recognizing that there is no such thing as the faculty of memory. ". . . the use of the word 'memory' in the sense of its being a distinct faculty is likely to lead to confusion." "There is no faculty of memory apart from the things remembered."

If a perception is in any way faulty, an imperfect image of it may be formed—or no image at all may be retained, if the perception is without meaning for the patient. Thus if a sensory perception is impaired early in life, say in one particular sphere, memory of events in that sphere of sensation will be poor: for example: A child with congenitally defective vision will have a poor visual memory. A child with congenitally

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defective auditory perception (i.e. auditory agnosia) will have no auditory memory. He will be quite unable to repeat correctly words said aloud to him (because of the imperfect perception of word sounds), and he will later be quite unable to recall what was said to him, even if he did appreciate its meaning at the time with the aid of visual and tactile associations. He will not have at his disposal a store of standard word symbols, but may make constantly changing sounds which have a significance, but only for himself (idioglossia), and have no permanent system.

When perception is faulty later in life, patients may have a good memory for distant past events, retaining, perhaps, an intact system of previous images and symbols, but they may not "take in," or remember, events in the recent past. Thus a patient with acquired auditory agnosia may not be able to understand a single word said to him, but may be able to talk to others perfectly well, using the store of well-formed word symbols, which existed before the onset of disease.

Destruction of images of perception and symbols causes faulty memory of past events in every sphere. Aphasia may be described as defect of memory in this sense.

Inability to integrate images and symbols may cause faulty memory, as occurs perhaps in senile dementia or other kinds of organic dementia—that is, the difficulty may be a purely conceptual one.

All the functions described above depend upon "memory" in the sense that they depend upon the ability to organize and integrate previously acquired images and symbolic forms.

Dr. Macdonald Critchley, in a recent communication to the Royal Society of Medicine (1951), has pointed out that one most striking clinical feature of patients suffering from defects of the nature described above is the *variability of performance*. "The patient may make a gross error one moment, and give a successful response the next. . . . These very irregularities, variabilities, repetitions, hesitances, changes of mind, erasions, and so on, are, I submit, important. . . . I regard this sort of phenomenon as characteristic."

Patients suffering from organic disease of the cerebral cortex are apt to show certain generalized patterns of abnormal behaviour. These have been noticed by several authors (Pick, 1909; Marie, 1906 and 1917), but particular attention has been paid to them by Goldstein, and he has described them in detail, most clearly in his latest work on language and language disturbances (1948).

These alterations in behaviour include:

(i) *Loss of the "categorical" or abstract attitude.*—The patient loses his ability to deal with abstract situations and is confined to the concrete.

Impairment of the abstract attitude may be demonstrated by means of:

(*a*) Sorting tests—such as Weigl's sorting test, when the patient may be able to sort the objects according to one property, e.g. colour, but he will be unable to conceive of another manner for sorting them.

(*b*) Tests regarding the patient's understanding of proverbs, allegories, and abstract nouns.

(ii) *A tendency to "catastrophic" reactions, and to a system of behaviour which will protect him from such reactions.*—The patient, when faced with a task which he is unable to perform, becomes agitated, may burst into tears, be angry, sullen or aggressive. The patient is unable to control such reactions. In order to avoid them, he may isolate himself from the world, or he may become excessively orderly, placing all his possessions with meticulous care in appointed places.

The patient is often quite unaware of his deviation from the normal. His adaptations are often effected without entering his consciousness.

Description of a Selection of Clinical Cases

Case 12621.—Dr. D. Williams' case. C. Y., male, aged 56, right-handed, well-educated, English speaking, business man.

This patient suffered from dysphasia, dyslexia, dysgraphia, dyscalculia, dyspraxia, disorientation in space, including right-left disorientation, and finger agnosia, visual disorientation, colour agnosia, grossly defective memory, and a defective power of abstraction. The defects were the result of syphilitic vascular disease, and the cortical lesions were probably multiple and bilateral.

On admission to hospital, the patient complained only of difficulty with vision, and a defective memory for a period of eighteen months.

History.—The story of his illness was one of sudden brief episodes of disability, which partly resolved, leaving, however, some symptoms which gradually became aggravated. Two years before admission, the patient had suddenly lost control of his right hand while shaving one morning. His hand was for a short time weak and shaky, but returned to normal. His vision then became suddenly blurred six months later, while he was walking down the street. He found he was unable to see out of the right side of his eyes. He denied any accompanying symptoms. Since that time his vision was poor. He was not able to read properly and long words confused him. His memory deteriorated slowly. At the time of examination he complained "I haven't got what it takes now, and am no longer a proficient business man." He had difficulty thinking of the words he wished to say. He often forgot what others had said to him. On account of his disabilities he retired from work. He sometimes felt very unsteady on his feet, and staggered about as if drunk. One year before admission, the razor dropped from his right hand while shaving, the right side of his mouth drooped, and when he tried to call his wife, he could not make any sound. He managed to get to bed unaided, and within a few hours his symptoms had disappeared. He remained in bed for four weeks. He complained of no other symptoms.

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On examination.—The patient appeared alert, co-operative and friendly.

Neurological examination revealed a complete right homonymous hemianopia, and visual disorientation in the left homonymous half-fields. The fundi were well defined and of normal colour, although there was some narrowing of the arteries. No hæmorrhages or exudates were seen. The pupils were irregular, the right larger than the left, and reacted minimally to light, but briskly on accommodation. There was a ptosis of the right eyelid. The cranial nerves were otherwise normal.

The patient exhibited a marked regular fast tremor of the outstretched hands and fingers, which persisted during movement. Rombergism was present, and the patient's gait was unsteady.

The reflexes (apart from the abdominal reflexes), were unobtainable. Plantar reflexes were flexor.

Sensory testing revealed a generalized patchy delay of appreciation of pin-prick over the entire body and extremities. Cutaneous sensibility was otherwise normal. Vibration sense and joint position sense were defective at the toes and ankles, but normal elsewhere.

General examination revealed no abnormality except for hypertension. The blood pressure was 210/100. The heart was not enlarged.

The patient was found to have strongly positive blood Wassermann and Kahn reactions, for which he was later given intensive treatment. The cerebrospinal fluid was normal, with negative Wassermann and Kahn reactions. The Lange showed no change. X-rays of the skull and chest were normal. The electroencephalogram was inconclusive, showing generalized intermediate slow activity.

Further examination disclosed the specific defects of function mentioned above. Detailed descriptions are here recorded.

I. Phasis.

(*A*) *Dysphasia.*—The patient's spontaneous conversation was somewhat disjointed. He said "Want to say something—can't think of it—got everything I want to say, but just can't say it—then goes out of my mind." During conversations he frequently used the wrong word, e.g. said "dentist" for doctor, and showed a slight tendency to jargon.

He was asked to name several objects.

Object	*Patient's response*
Pencil	Correct.
Matchbox	Long pause, then the patient said triumphantly: "Box of matches. Took me some time to think it, there it is."
Match	Correct.
Head of the match	"That's the . . . the . . . I've used it many a time—say it, will you? I know it but I can't think it out . . . Matchbox—box . . . Directly you'd mention it I'd say Yes, that's it, or I'd say No, it isn't . . . matchbox . . . "
Asked "Is it the matchstick?"	"Yes . . . No . . . box . . . case . . . match case . . . directly you'd tell me I'd agree *or* I wouldn't agree. At the moment I can only think of matchbox. . . . Give me a matchbox."
Asked "Is it phosphorous?"	"Yes—but we never call it that."
Asked "Is it the match head?"	"Yes"—rather doubtfully.
Glass of water.	"Can't do it—glass—glass of—Oh, common thing like that . . . glass of water."
Tea in a cup.	Correct.
Ashtray.	Matchbox . . . match . . . "
Asked "Is it an ashtray?"	"Yes . . . that's it, ashtray . . . "

Handling of the objects did not assist the patient to name them.

The patient thus showed some difficulty with the *naming of objects*, and some perseveration of speech.

He was asked to define the meaning of the word "accident." He said: "Some body falls off a door, breaks their neck."

He was asked: "What is a door?" He replied: "Of course not a door that opens and closes, a chair, a chair, I mean."

The patient's response showed he understood the meaning of the word "accident," but only in its concrete application. He could not define it as an abstraction.

(*B*) *Comprehension.*—The patient was asked to perform some simple tasks.

(1) "Take the ashtray and put it next to the lamp." He did this correctly.

(2) "Sit down." The patient did so.

(3) "Fold this piece of paper neatly and give it to me." The patient was able to do this, although he folded the paper clumsily.

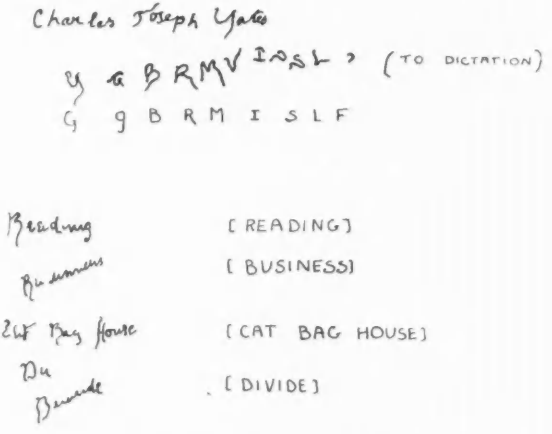
He could thus understand simple words and sentences.

When asked to do more complicated tasks, however, or to define more difficult words, he became confused. He complained "he could not understand."

He thus suffered from a moderate defect in the comprehension of speech.

II. Writing.

The patient showed considerable dyspraxia for all forms of movement in the right hand. His writing is shown here.



III. Spelling Aloud.

The patient was asked to spell the following words aloud:

Word	*Patient's reply*
Basket	BASCATE
History	Correct
Saucer	Correct
Difficult	Correct
Scissors	Correct
Divide	Correct

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The patient thus suffers from *dysgraphia.* Spelling aloud is only slightly defective.

IV. Reading.

(*A*) *Letters.*—Patient read A, B, F, E, H, G, correctly but very slowly. When shown "D," patient said "A," hesitated, said "My heavens above," and finally said "D."

(*B*) *Words.*—

Cat: patient read this as CART – CUT.

Bag: patient read this as BAS. "Oh dear, what is it?"

After training, patient could read this as BAG.

House, Game, Lame, Cake; patient could read all these very slowly, sometimes confusing the letters, for example, "S" for "M."

(*C*) *Sentence.*—"I went into the garden." Patient read this as "I wilt into the garden."

The patient was able to explain the meaning of the words he read.

The above testing demonstrated a mild *dyslexia.*

V. Gesture and Mime.

The patient did not use his right hand for any spontaneous gesture.

When asked to shake his fist and wave goodbye, he was able to do so, although very awkwardly. Similarly, any pantomime (such as showing how he would play the piano, comb his hair, and so on), was very clumsily performed. The patient seemed to have the correct idea, however, of what he was expected to do.

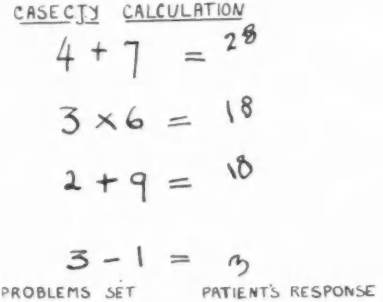
VI. Song.

The patient could sing "God Save the King," and "Auld Lang Syne," with approximately correct tunes. He could not manage to sing all the words, however, and often substituted a hummed note or two in place of them.

VII. Calculation.

The patient could correctly write and say aloud numbers 1–10.

He could correctly calculate in his head "three multiplied by five equals fifteen," and other very simple sums. His written performance of calculation, however, was as follows:



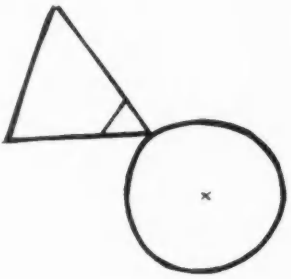
He was unable to perform more difficult problems mentally. For example:

Question	*Answer*
How many pennies in half a crown?	28.
Take 7 from 100?	97, no, let me see, 91.
And 7 from 91?	86.

The patient therefore showed *asymbolia* for mathematical symbols and some *dyscalculia.*

VIII. Voluntary Movement.

(*A*) The patient was noticed to be extremely clumsy with his right hand. He complained spontaneously that he had great difficulty with dressing. He said "I always do things the wrong way. . . . I have a tendency to cross over . . . my right foot goes on my left foot . . . All that nonsense that you know is wrong, but just can't seem to do right."



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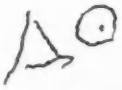
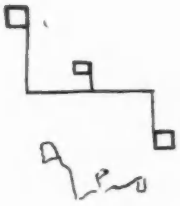


CASE CIY PATIENTS COPY OF DESIGN



2 DESIGN TO COPY

2 PATIENT'S COPY

CASE/CIY PATIENTS DRAWING OF A DAISY HEAD

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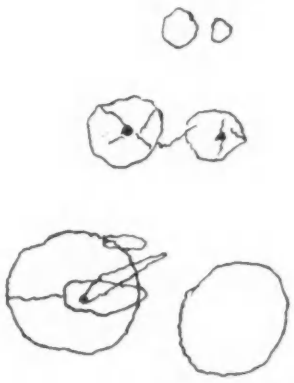


CASE C.IJ ATTEMPTS AT DRAWING A BICYCLE

CASE C.IJ PATIENT'S MAP OF ENGLAND

The patient was unable to put on his dressing gown correctly. He fumbled, and tried to put it back to front. He was unable to tie the cord of his gown, and could not button his pyjama jacket. He put on his spectacles upside down.

He thus suffered from *dressing Apraxia*.

(*B*) *Writing and drawing.*—The patient complained that his writing and drawing was all performed on a very small scale, which he thought was part of his trouble. "Why I do it that way, but there it is . . . I have to do it crowded, small. . . . " Examples of his writing have been shown above. Examples of his drawing are now included.

(*C*) *Construction.*—(*i*) *Goldstein stick test:*

(*a*)

The examiner chose a stick of a certain length. The patient was asked to choose from a number of sticks one of similar length, and place it in the position shown on the left. He was quite unable to chose a stick of correct length.

(*b*)

The patient was asked to copy the pattern shown, which was placed in position by the examiner. The patient chose sticks of incorrect length and tried to put his sticks on top of those of the examiner. Then he placed them in this manner:

First attempt

Second attempt

He was told to take one short stick and one long one. He took a third long one, and made the following pattern:

(*c*)

He was then given two sticks of the correct length and told to copy the pattern shown here. The patient made an attempt:

(*d*)

The patient was again asked to choose two sticks from the pile and copy the pattern of the examiner, which is shown here. He chose two long sticks and placed them thus:

The above test demonstrates *dyspraxia* and visual *disorientation.*

(*ii*) The patient was asked to name certain shapes made with sticks.

(*a*)

The patient ran tentatively through the following list of names: Parallelogram, Isosceles triangle, three-sided square. He then enquired with charm: "Is there such a thing as a three-sided square?"

He was asked: "Is this a triangle?" He replied "Yes" with great enthusiasm.

XUM

(*b*) The patient called this "A four-sided square—no—not quite."

He was then asked "Is this a rectangle?" He replied "Yes."

(*c*) The patient called this a "four-sided square."

(*d*) He was then asked to construct a triangle with sticks. He made the following pattern:

This test demonstrates dysphasia and dyspraxia.

(*iii*) *Kohs' blocks:* The patient was quite unable to perform even the simplest forms of this test, partly on account of dyspraxia and partly because he was visually disorientated and suffered from colour agnosia. In attempting to perform this test, the patient placed his blocks on top of the pattern he was asked to copy.

(*iv*) *Raven's matrices:* The patient was unable to perform more than the first two of the progressive matrices and these only with great difficulty, after several explanations and demonstrations of what he was supposed to do.

IX. Colour Gnosis.

Colour matching was better performed by the patient than colour naming, but several errors were made in both tests. Thus a dark red was on one occasion matched to a dark green, and occasional confusions were made between grey, light blue and light green.

Colour naming was very poorly performed, the patient being quite confused, calling a blue colour red, or green, or black, and so on, without any consecutive consistence.

When asked how many colours there were in a bowl of flowers (there being three, white and yellow petals and green leaves), the patient said "Half a dozen," very boldly, and then added "It's an absolute guess, you know."

The patient thus suffers from colour agnosia.

X. Pictures.

On being shown pictures, the patient was able to grasp the whole of certain scenes, e.g. a racecourse; but on being shown a map of England, he recognized it only in portions, thus demonstrating *simultanagnosia.*

He was not able to grasp the meaning of cartoons or pictured jokes without captions.

XI.—Orientation of the Body in Space.

(*A*) *The patient's knowledge and understanding of the parts of his own body and his orientation as regards right and left.*—The patient was unable to tell which was his right and which was his left, and admitted he "Couldn't really say. If I were to say, it would be just a guess." He was also unable to tell which finger was which on either hand. For example, when asked to show which was his right index finger, he showed his left ring finger, and so on.

He thus suffered from right-left disorientation and finger agnosia.

The patient was asked to touch his right ear, his nose, his left eye, his right wrist and other parts of his body. He responded in a confused manner, often making mistakes, e.g. when asked to touch his nose, he touched his eye, when asked to touch his ear, he touched his mouth. His mistakes were partly due to his defective comprehension, and partly to agnosia for different parts of the body.

Even when he did understand the meaning of what he was asked to do, he hesitated, was very uncertain, and sometimes confessed he could not think of the correct position of the part of the body he was asked to touch. He frequently perseverated—that is, when asked to touch an ear, he touched his nose. When asked then to touch an eye, he again touched his nose. He thus suffered from *autotopagnosia.*

(*B*) *Orientation of the patient in relation to his environment.*—(i) *Visual orientation:* The patient complained spontaneously that there was something wrong with his eyesight, but he didn't know what it was. He said on testing he could see only half things, but that in life he saw everything whole, including people's faces. He had a *right homonymous hemianopia,* as has been stated above. He was unable to localize the position of stimuli correctly in his left field. This was tested with solid objects, e.g. the examiner's hand, and also with a bright light. The patient failed to localize the stimuli in both cases.

(ii) The patient was asked to count a number of objects scattered on a table before him. (The objects were within his left field of vision.) There were 10 objects, but the patient repeatedly counted 12, 14, 7, and was unable to gauge the correct number. If he was allowed to touch and remove each object as he counted it, he was able to give the correct number.

(iii) The patient was asked to choose the nearest to him, the farthest from him, the farthest on the left, the farthest on the right, of a number of objects scattered on a table before him (all objects being within his left field of vision). The patient was very hesitant, and finally said he was unable to understand the meaning of the expression "nearest to himself." He chose various objects quite at random, with no relation to the correct situations, and confused right with left again.

(iv) The patient was asked to sort a series of objects according to their shape—triangles, diamonds, circles and squares. He was unable to do so by vision alone. When allowed to handle each object carefully, he was able to sort them accurately.

XII. Memory.

(*A*) *Auditory memory.*—The patient was asked to memorize the following words, which were said aloud to him, and which he was able to repeat aloud correctly: "PENCIL, BLUE, and TWELVE PICCADILLY." After an interval of fifteen minutes, during which he was occupied with other tests, he was asked to recall the above words. He said "Not the faintest idea." He was asked "Was one word a colour?" He replied "No."' He was asked "Was one word 'blue'?" He said "No." He was asked "Was one word 'pencil'?" and answered "I couldn't say." He then suddenly said "Twelve Piccadilly." The above test was repeated at intervals during the next hour or two, and again next day. The patient failed at all times to remember all words correctly.

He thus suffered from *defective auditory memory.*

(*B*) *Visual memory.*—The patient was shown a simple design drawn on paper, and asked to look closely at it for a few moments. The design was then withdrawn, and the patient was asked to reproduce it. As he suffered from dysgraphia and dyspraxia, the results were, of course, poor, but, in addition, a defect of visual memory was obvious. The patient made several attempts to reproduce a design which he had previously been able to copy, but was unable to do so accurately.

He was also unable to recall words he had previously read, although at the time of reading he had said he understood the words.

XUM

He was asked to repeat the Babcock sentence. He still made various errors after the sixth attempt.

He was asked to name the present King and the previous Kings of England. He said (*a*) "George V"; (*b*) "The rascal who went off"—and could name no others. He knew the name of the Prime Minister.

XIII. Intelligence Testing.

This was performed on the patient by the hospital psychologist, Dr. McFie. The report read as follows:

"The patient's vocabulary, still well preserved, indicated a previously very superior intelligence with an I.Q. of the order of 140. Other performances were impaired by his special disabilities: similarities, and digit span, by his dysphasia; picture completion by his dysgnosia; arithmetic by his discalculia and block design by dyspraxia."

XIV. Conclusions.

The above tests indicate the patient suffered from dysphasia, dyslexia, dysgraphia, dyscalculia, dyspraxia, disorientation in space, including right-left disorientation, and finger agnosia, visual disorientation, colour agnosia, and a grossly defective memory.

Case 15249.—Dr. McArdle's case. A. R., female, aged 52, right-handed.

This patient was admitted with no complaints except headaches, which had begun a few months before admission, and poor memory. She lacked insight into her other defects.

On examination, she was found to have bilateral blurring of the discs, an incomplete left homonymous hemianopia, slight impairment of the sense of position in the left big toe, and slight increase of the left knee and ankle-jerks. There was also slight astereognosis in the left hand, without impairment of position sense or two point discrimination.

She showed marked spatial disorientation, readily lost herself even in familiar surroundings, and even had difficulty in finding her own bed in the ward, which she only identified by seeing her possessions on the locker beside it. She had difficulty in judging the relative distance of objects, especially if they were far away. She also had great difficulty with any constructive work which involves spatial relationships, especially where three dimensions were concerned. She made numerous mistakes in drawing cubes, triangles, and other figures, and also in copying more complicated patterns. She was quite unable to draw a map of areas previously very familiar to her.

The patient was examined by the psychologists, Mr. Zangwill and Dr. McFie, who reported: "Verbal tests showed the patient to have been of high-normal intelligence with an I.Q. about 125. Tests for learning ability, verbal retention, and the tendency to patterning in her performances of Weigl's sorting test, indicated a mild degree of organic deterioration."

The patient was found to be suffering from a large parieto-occipital tumour, which was removed at operation, and proved to be a meningioma.

She made a good post-operative recovery, although she continued to show some disorientation in space thereafter.

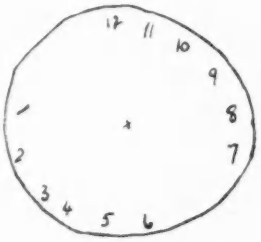
The patient's difficulty in coping with spatial relationships is shown in the following tests:

Case 13133.—Dr. McArdle's case. F. P., male, aged 49, right-handed. Business man.

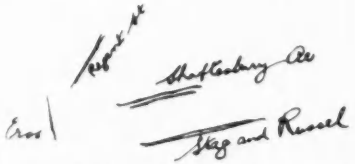
This patient was admitted to hospital with the history of progressively increasing difficulty with speaking, writing, reading, and calculation. The symptoms were first

noticed some five months before admission. He was discovered to be suffering from the effects of a tumour in the left temporo-parietal region of the brain, which proved to be a glioma.

Neurological examination revealed few abnormalities, apart from dysphasia, dyslexia, dyscalculia, and defective orientation in space. The patient was markedly



CASE AR PATIENT'S DRAWING OF A CLOCK FACE



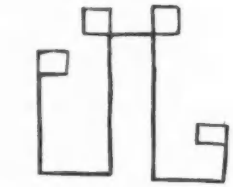
CASE AR PATIENT'S MAP OF PICCADILLY CIRCUS

CASE AR DESIGN TO COPY

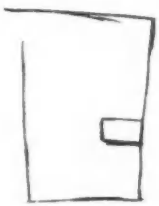
PATIENT'S COPY

dysphasic, often at a loss for words to express himself, constantly making excuses, being tremulous, nervous, and emotional. He often used a wrong word, sometimes a jargon word. He also suffered from a mild defect of comprehension of speech.

The following tests indicate his defective writing, spelling and calculation. His defective orientation in space is also demonstrated by his drawing of the map of England, and the mistakes he made with compass directions.



CASE 8R DESIGN TO COPY



PATIENT'S ATTEMPTS

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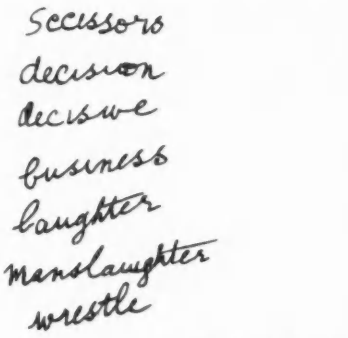
Case 27743.—Dr. Critchley's case. Dr. J. K., male, aged 52, right-handed. Research physicist.

This patient, a highly intelligent mathematician, was admitted to hospital complaining that for the previous five months he had slowly, but progressively, been finding his work increasingly difficult; his speech had become halting, and he could not always express himself clearly; his memory had become more and more defective.

Neurological investigation revealed a weakness and clumsiness of the right arm and leg (more marked in the leg), and diminished sensory appreciation for all



CASE A.R. WRITING AND SPELLING
(TO DICTATION)

CASE A.R. PATIENT'S DRAWINGS

A TRIANGLE TWO PARALLEL LINES

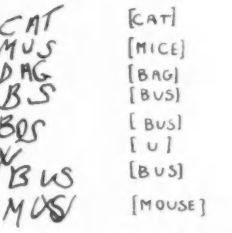
A BICYCLE AN EQUILATERAL TRIANGLE

forms of sensation on the whole of the right side of the body. There was tactile inattention to a marked degree on the right half of the body.

In addition, the patient showed a pronounced defect in the understanding and use of abstract symbolic forms, such as mathematical figures and signs, letters, punctuation marks, and so on.

The patient's speech was slow, and he tended to stutter. From time to time he was silent for several moments, saying he could not think of the correct word to use, or again, he could think of the word, but had difficulty "bringing it out."

His handwriting had become childish, and his spelling was defective.

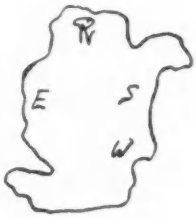


CASE F.P. PATIENTS WRITING AND SPELLING [TO DICTATION]

1

CASE F.P. PATIENTS ATTEMPTS TO DRAW A BICYCLE

2



CASE F.P. PATIENTS MAP OF ENGLAND

The patient complained spontaneously that his greatest difficulty in speech was with the letters "S" and "F." He complained that these letters also were difficult to write, and he became confused regarding the difference between "ph" and "f" in the spelling of a word.

Examples of the patient's writing are given here, demonstrating:

(1) The childlike quality of the handwriting.

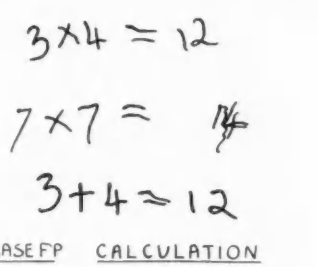
(2) Defective ability to spell and punctuate.

Other tests are included which demonstrate the patient's inability to use mathematical symbols, with which he was previously very familiar.

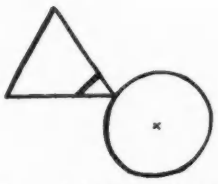
The patient's defective power of abstraction is also shown.

The patient was asked to punctuate several paragraphs such as the one quoted here:

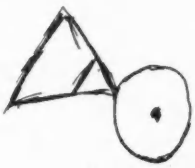
> it is strange said the professor that there are only seven students here today where are the others lost i fear said the boy



CASE FP CALCULATION



CASE FP DESIGN TO COPY



PATIENTS COPY

The patient inserted quotation marks as follows:

> "it is strange," said the professor; that there are only seven students here today where are the others; "lost i fear" said the boy.

The patient was asked to write the letter "A" as a capital letter and as a small letter. He was able to write a capital "A." When he came to write the small letter he hesitated some time. He then wrote down the word "and" in small letters, looked at it, and copied down the letter "a" separately.

The patient was asked to write the word "cat" first in brackets and then in inverted commas. He wrote: cat); cat."

Mathematical symbols.—The patient was somewhat confused regarding the meaning of the signs.

He could not always read them correctly nor write them down to dictation. He was asked to write down in symbol form seventy-four divided by a hundred.

He wrote:

74 : 100
74/100
74
100

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Sussors	[SCISSORS]
Büsineso	[BUSINESS]
Scarlet	[SCARLET]
Disciuon	[DECISION]
Precise	[PRECISE]
Precuon	[PRECISION]
Physucian	[PHYSICIAN]
Trumph	[TRIUMPH]
Fic	[PHYSICS]
Physico	["]
Phyic	[PHYSICIST]
Fluesence	[FLUORESCENCE]
Polyglot	[POLYGLOT]
Discussuon	[DISCUSSION]
Monarcy	[MONARCHY]

CASE J K PATIENTS WRITING AND SPELLING [TO DICTATION]

He was asked to write the sign for division.

He wrote:

He was asked to write x cubed in symbol form. He wrote $X^{\frac{3}{3}}$ after a long pause for thought.

The patient was unable to read aloud correctly the following equation:

$$(A^2 \times B^2)^3 \times G - X^2 = S.$$

The patient was asked to write "4" in Roman figures. He could not at first think what Roman figures are, then drew a clock face and wrote

VI IV (in place of the IIII usually present on clock faces)

The patient was asked to name the common factor in the following equation:

$$\frac{(27A - 3B)(X^2) + (48M - 27B)(X^2)}{74} = \frac{(17 + 46)(7R - X)(X^2)}{62}$$

He was unable to do so. When asked if it were (X^2) he said "Yes, of course." With simpler equations he could correctly name the common factor.

The patient was asked to make as many three-letter words, and as many four-letter words, as possible, from the following letters:

R I I S E M Y T A

The patient wrote TEA, SIT, MET, TEAM, REST. He could not manage to write any others. This took him twenty minutes.

The patient was asked to regroup the following letters, so as to form intelligible words:

(1) M B A L

After a long pause the patient was able to write BALM, and also, again after some time, could write LAMB.

The patient was asked to regroup

(2) H S U R B to form a word (BRUSH).

He was unable to do so; after ten minutes' struggle, he gave up the attempt. He was asked to regroup the letters:

(3) T S E A L to form three words.

He was able to write STEAL and LEAST, but not SLATE.

These tests demonstrate difficulty with the performance of *abstraction*.

Discussion

It has been stated earlier that the functions which have been described are dependent upon perception, which phenomenon includes immediate sensory perception of sensory stimuli, the formation and integration of (1) images of sensory perception, (2) the symbolic representation of such images, and (3) systems of abstractions derived from symbols. Perception, itself, however, is an individual experience. Each of the functions mentioned above involves perceptions, images, and symbols, of multiple categories of sensation. Language involves them all, being the means by which man attempts expression of all his experiences, and communication with others who would express their experiences to him.

If the various types of dysfunction which have been described are examined in the light of their being disorders of aspects of perception, it is suggested that the nature of the dysfunction may be expressed in terms related to perception, as it has here been defined. That is to say, the defect of function may be referred to:

(1) Imperfect immediate sensory perception.
(2) Defective images of perceptions.
(3) Defective images of symbolic representations.
(4) Defective images of symbol abstractions.
(5) Defective power of abstraction, integration, and association of perceptions and symbols.

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It may be concluded from the above descriptions that the human organism is capable of performing certain "mental" functions which depend upon the ability to perceive sensory stimuli, to differentiate, select, abstract, and give to them symbolic representations, and finally, to compare, deduce and think in categorical terms. There exists here a relation between mental and physical phenomena, dependent upon dynamic activity on the part of neural tissue.

It has been mentioned above that the precise nature of sensory stimuli before they are perceived is not known. Stimuli are no doubt transmitted in some "symbol form." One cannot imagine, for example, visual stimuli transmitted by neural tissue in the shape of photographic images, nor sounds as such, nor smells. It is here suggested that what the organism perceives are dynamic patterns, or rhythms, which are generated and transmitted by neural cells. That is to say, a sensory stimulus may result in the generation of a specific rhythm, or cause a change in an already existing one. Such a rhythm acquires a significance in an individual following its repeated transmission. In the newly born and the young, patterns of rhythm may be simple and crude, and become later more and more complex. Rhythms may be abstracted in the manner already described, and may be condensed and given symbolic representation. Rhythmic activity is known to be present in nerve tissue, as demonstrated by electroencephalographic records. Adrian (1941 and 1950) has shown that basic electrical rhythms are generated by the thalamus. It is not, however, suggested that the rhythmic patterns which precede perception are necessarily electrical in nature.

It has been emphasized above that the functions described are not isolated performances. They are the complex result of the organization and integration of many functions. No attempt, it would seem, should therefore be made to "localize" any single function to a specific area of neural tissue. This paper began with the remark, however, that "organic disease of that part of the human cerebral cortex which lies posterior to the central fissure of Rolando gives rise to a variety of specific disturbances of function. . . ."

In the adult brain there does indeed appear to be a certain organization of function in the cortex. We know that language and associated faculties are, as a rule, affected by lesions in that part of the cortex which lies posterior to the central fissure in the dominant hemisphere. Similarly, spatial orientation is affected by lesions in a corresponding area in the minor hemisphere (Paterson and Zangwill, 1945; McFie, Piercy, Zangwill, 1950). We know also, however, that when one hemisphere is damaged in infancy the other hemisphere may competently "take over" its supposed functions, so that a right-handed child with a damaged and unfunctioning

left hemisphere may have excellent powers of language (Gooddy and McKissock, 1951). We know that leucotomy may temporarily abolish an intractable pain in a patient, but that after an interval—usually of a few months—the pain generally returns. It must be assumed that certain cells transmitting the "pain pattern" are ablated by the operation and that later the pattern is reconstituted by other cells. It is thus necessary to suppose that brain cells are capable of a variety of performances, that almost every cell or group of cells performs multiple functions, but that certain particular groups of cells are more liable to perform certain functions. One may assume that the likelihood of particular cell groups performing specific functions is determined by evolution. The later the development of a group of cells, the more highly evolved are its patterns of functions. "Localization" depends upon those groups of cells which perform the final integration and organization of the widespread cerebral activity necessary for the performance of every separate function.

The brain, therefore, should be regarded as a very plastic, constantly changing structure. Perceptions, dependent upon brain function, are equally supple and crescent.

Finally, it should be emphasized that while the events which lead to perception may be described in physical or chemical terms, perception itself is an experience which belongs to the individual who perceives. It is not a quantitative but a qualitative phenomenon. The affective states which are an integral part of perception belong also to individual experience. These qualitative phenomena are independent of space and time, although evoked by events which do have spatial and temporal attributes. Such phenomena belong therefore to a different category than do material phenomena.

Summary

The disorders of function which result from organic disease of that part of the human brain cortex which lies posterior to the fissure of Rolando are discussed. These disorders are stated to be related to the perception of stimuli concerned with vision, hearing, the sensations of touch, pain, posture and vibration, stereognosis, tactile discrimination, language in all its aspects, calculation, voluntary movement, the awareness of the body, and its orientation in space and time.

The faculties of language, voluntary movement, calculation, the orientation of the body in space and time, colour gnosis, and memory are analysed and discussed.

The hypothesis is put forward that the functions discussed above depend upon perception, and it is suggested that each dysfunction may be related to a particular aspect of disordered perception. It is suggested

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that the organism perceives rhythmic patterns of cerebral activity. Perception is defined as a phenomenon which involves a series of events which may be scientifically described, but which is itself the qualitative experience of an individual.

ACKNOWLEDGMENTS

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THE PHYSIOLOGICAL EFFECT OF VARIATIONS IN THE STIMULUS FREQUENCY ON THE MOTOR CORTEX OF THE MONKEY[1]

BY

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ALTHOUGH each of the recent workers in the field of cortical stimulation is aware of the fact that variations of the different parameters of the stimulus is of importance for the result obtained, little systematic work on the significance of frequency of stimulation is available. Hines and Boynton [11] suggested already in 1940 that the frequency may be used "to isolate the activities of functional units" and to separate pyramidal from non-pyramidal discharges. Bailey and von Bonin [1] and later Livingston [12] observed that the muscles of the tongue responded to lower frequency of stimulation than those of the face. The most striking effects of variations in frequency were obtained by Nulsen *et al.* [16], who with lower frequencies inhibited and with high frequencies of stimulation applied to the anterior cerebellar cortex facilitated movements induced by stimulation of the motor cortex. The present work is concerned with the influence of frequency of stimulation of the motor cortex on skeletal muscles whose responsiveness was indicated by EMGs.

METHOD

The experiments were performed on 10 monkeys (Macaque and Cynemolgus) in "Dial"-urethane anæsthesia (0·45 c.c./kg. i.p.). Extensive craniotomy exposed the Motor cortex which was kept warm with saline and oil during the experiment. Mono- or bi-polar silver electrodes mounted in the holder of the Horsley-Clarke apparatus were used. This procedure permitted re-stimulation of the same point repeatedly after other cortical sites had been excited. A Goodwin stimulator delivered condenser discharges of independently variable duration, frequency and voltage. The duration used was 7·7 m sec. per pulse, the voltage just slightly above threshold unless otherwise indicated. The stimulation was appled for 3–8 seconds (constant in a particular animal), every two or, in occasional monkeys, three minutes. The frequency was

[1]The studies were aided by a contract between the Office of Naval Research, Department of the Navy and the University of Minnesota.

varied between 10 and 102 impulses/sec. Only those experiments in which results were duplicable over a period of hours are considered. Area 4 was stimulated exclusively.

The pattern of response in a group of six muscles was recorded electromyographically, the electrodes being insulated wires with short bared portions which were sewn through the muscles for bi-polar recording, with an inter-electrodal distance along the muscle of about 1 cm. The position of the electrodes was checked at the beginning of the experiment by stimulating faradically through the 2 members of each pair and observing the response; final verification of placement was obtained by post-mortem examination. Amplification and recording was made with an Offner push-pull amplifier and inkwriter. For further detail cf. earlier publication from this laboratory.

Results

(1) *The effect of varying frequencies of stimulation on the response of skeletal muscles from different cortical sites.*—If a cortical site is stimulated with a certain voltage and duration of impulse but at varying frequencies, the response as recorded electromyographically may change, some muscles responding better to a lower frequency and others to a higher frequency. Fig. 1 represents such a shift in pattern of response as recorded in biceps brachii and triceps from a cortical site in the arm area. As can be seen, the triceps EMG is larger in response to lower frequencies of cortical stimulation (A–C), while the biceps responds with the largest

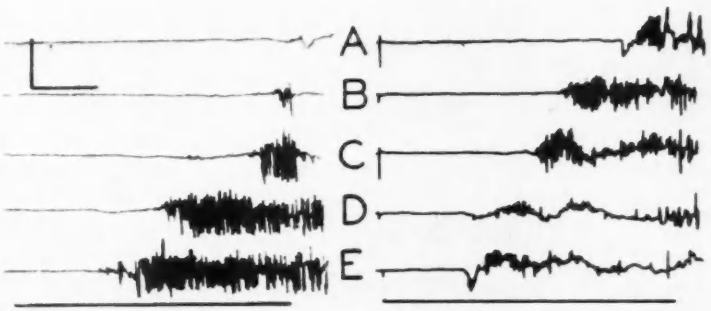

Fig. 1.—*Effect on EMG response of arm muscles of stimulation of a cortical site at a series of frequencies.* Cynemolgus monkey; site in arm area 4 (10 mm. lateral to mid-line). Left: biceps brachii; right: triceps brachii. A–E 1·8 V., stimulation for 4·5 sec., pulse duration 7·7 sec. Stimulus frequencies: A, 33/sec.; B, 42/sec.; C, 53/sec.; D, 66/sec.; E, 83/sec. Calibration: 1 sec. and 300 microvolts in all figures unless indicated otherwise. Horizontal lines beneath EMG's indicate duration of stimulus. Elbow fixated at 160 degrees; wrist free.

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amplitude at the two highest stimulus frequencies. It is of interest to note the decrease in "latent period" in both muscles with increased frequency of stimulation, indicating that the relative amplitude of EMG responses does not necessarily parallel summation time. Thus, triceps responds earlier after application of stimulation at higher frequencies although its EMG was smaller than the more delayed response obtained with low frequency stimulation.

It is obviously very difficult to determine in which part of the central nervous system this frequency selectivity resides. An attempt was made by studying the frequency series at several cortical sites. Many such series of experiments demonstrated that the pattern of response to low and high frequencies at one cortical site might be quite different from that obtained at another site.

In fig. 2 an example of the response pattern to two stimulus frequencies at three cortical sites is shown which is selected from a larger frequency series, the records chosen for illustration from the series representing the general characteristics of the sites. The 3 sites are located just anterior to the central sulcus 10 mm. (B,B′), 13 mm. (A,A′), and 16 mm. (C,C′), from the mid-line. From all sites distinct responses of the biceps and

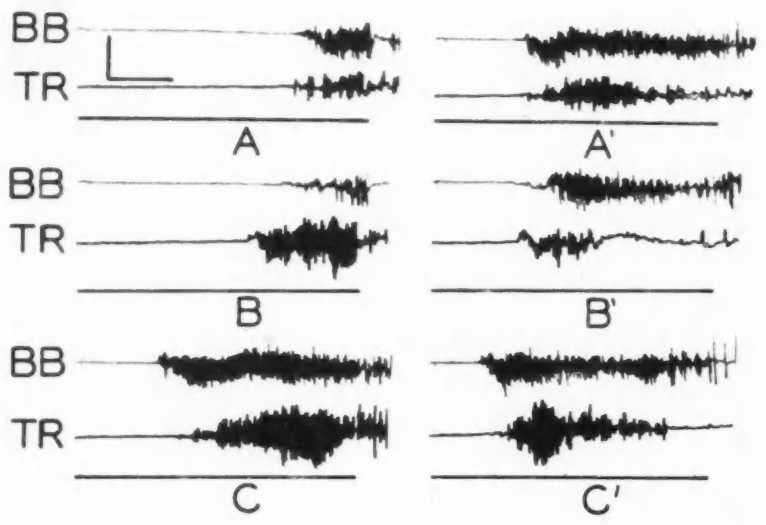

FIG. 2.—*EMG response pattern in arm muscles to stimulation of three cortical sites in area 4 at different frequencies.* Cynemolgus monkey; BB, biceps brachii; TR, triceps. A,A′ site 3 (location: 13 mm. lateral, near sulcus), 2·1 V. B,B′ site 1 (location: 10 mm. lateral, near sulcus), 2·1 V. C,C′ site 4 (location: 16 mm. lateral, near sulcus), 3·0 V. A–C at 42/sec.; A′–C′ at 83/sec. Calibration as in fig. 1.

triceps are obtained but frequency response of the same muscles is quite different from different sites. Thus the triceps response increases in amplitude and duration with increasing frequency at site A but decreases in both respects under these conditions of stimulation when sites B and C are stimulated. Moreover, it is seen that the frequency characteristic of one muscle is not typical for that of another muscle activated from the same cortical site. Thus from site B the responsiveness of the biceps increases with increasing frequency whereas that of the triceps decreases. Another example illustrating this phenomenon for some foot muscles also is shown in fig. 3.

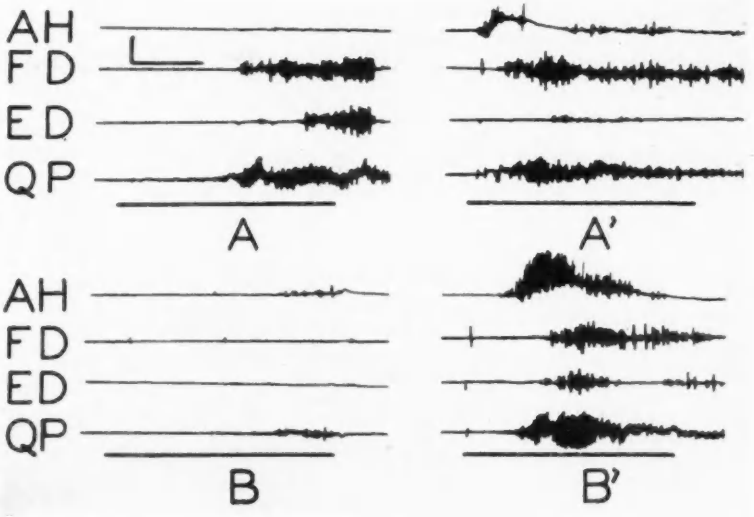

FIG. 3.—*EMG responses of leg to two frequencies of stimulation at two cortical sites. Macacus rhesus.* AH, adductor hallucis; FD, flexor digitorum longus; ED, extensor digitorum longus; QP, quadrator plantæ. A,A′ site 1, 1 mm. lateral; B,B′ site, 2, 4 mm. lateral; both sites just anterior to sulcus. A,B 33/sec.; A′,B′ 83/sec. and 3·0 V. Hip fixated 45 degrees, knee 45 degrees, ankle 65 degrees. Time line 2 sec.

A summary of two extensive experiments of this kind is given in Table I. Experiment A is based on the reactivity of 9 leg muscles activated by stimulation of 4 different sites in the contralateral area 4. Of 31 groups of frequency responses only one muscle from one side showed no distinct changes in the EMG with increasing frequency of stimulation; of the remaining 30 groups almost half (14) showed the largest response with the high frequency (82 or 102/second) while 9 showed the maximal amplitude of the EMG on low frequency stimulation (about 30/second).

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TABLE I.—FREQUENCY RANGES INDUCING LARGEST EMG'S IN A SERIES OF HIND-LEG MUSCLES ON STIMULATION OF DIFFERENT CORTICAL SITES IN TWO MONKEYS (MACAQUE)

Experiment A

Site	*a.h.*[1]	*f.h.b.*[2]	*f.d.l.*[3]	*t.*[4]	*b.f.f.*[5]
1	low*	low	high	high	high
3	low	low	low	(low)	high
6				high	mid
7	low	low	mid	low	high

Site	*s.*[6]	*g.*[7]	*r.f.*[8]	*sa.*[9]
1	high	high		high
3	±	mid	mid	high
6	high	mid	mid	mid
7	high	high	high	

Experiment B

Site	*r.f.*[8]	*b.f.e.*[10]	*b.f.f.*[1]	*gr.*[12]
C	high		low	low
G	low	high	low	
B	low		low	±
H	low	high	(low)	
D	low	high	low	±

Site	*s.*[6]	*f.d.l.*[3]	*e.d.l.*[11]
C	high	(high)	
G	±	low	low
B	high	low	low
H	±	low	low
D		high	low

[1] abductor hallucis; [2] flexor hallucis brevis; [3] flexor digit. longus; [4] tibialis; [5] biceps femoris (flexor); [6] soleus; [7] gastrocnemius; [8] rectus femoris; [9] sartorius; [10] biceps femoris (extensor); [11] extensor digit. longus; [12] gracilis.

*Low indicates 27,–33,–42/sec.; mid, 42, 53, 66 sec.; high, 83, 102/sec. was range giving largest response. Terms in parenthesis are for sites at which the muscle's response was not consistent. ± = no change in amplitude with varying frequency.

Of the 29 groups of responses recorded in experiment B 26 showed a distinct frequency response but only 8 showed the largest EMG with the higher frequency.[1] Obviously the optimal response with medium and even low frequencies is not uncommon with skeletal muscles.

One interesting feature of this series (cf. experiment B) is the difference in frequency optimum for the two functionally different parts of biceps femoris, the flexor portion responding with greater amplitude to low frequencies of cortical stimulation and the extensor part to higher

[1]In this experiment only low frequencies (27 and 33) second and high (83 and 102) were tested.

frequencies. In another animal this difference between the two parts of this muscle was confirmed.

The experiments demonstrate that not all muscles respond maximally to the same frequency of stimulation of a particular cortical site, and further that a frequency which may induce an optimal response in a muscle when applied to one cortical site may be less effective for that muscle at another cortical site than a higher or lower frequency.

(2) *The frequency effect at different intensities of cortical stimulation.*—A group of experiments was performed with frequency series at different intensities in order to determine whether the frequency characteristics described in the preceding section depend on the voltage used. The results seem to indicate that the relative pattern of response indicated by the EMGs of several muscles at different frequencies of stimulation is not altered by variations in voltage. This is shown in fig. 4 for a cortical site which on stimulation at a low frequency (33/sec.) elicited a large response in biceps (flexor part) and a lesser EMG in tibialis anticus, whereas at a high frequency (83/sec.) tibialis responded

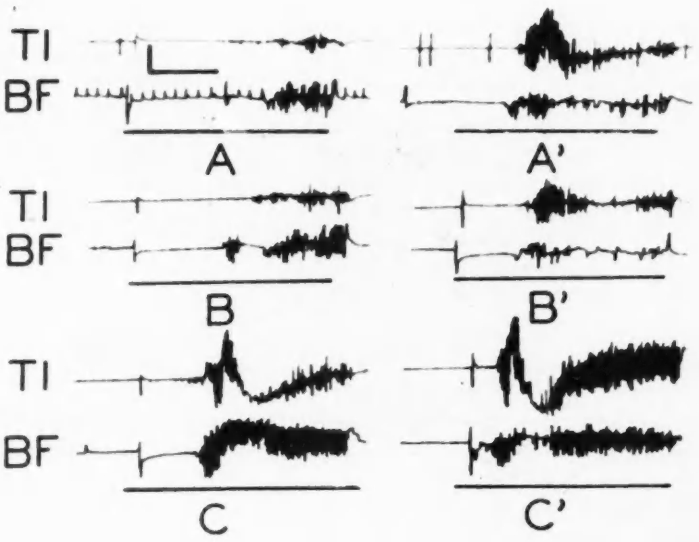

FIG. 4.—*EMG's produced by stimulation of a cortical site with two frequencies and several intensities.* Cynemolgus monkey. TI, tibialis anticus; BF, biceps femoris (flexor part). Site in leg area 4; leg fixated with hip 90 degrees, knee 160 degrees, ankle 160 degrees. A–C at 33/sec.; A′–C′ at 83/sec. A,A′ 3·5 V; B,B′ 4·9 V; C,C′ 6·3 V. Calibration as in fig. 1.

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better than did biceps femoris. The records of fig. 4 show that this relationship is independent of increases in voltage from 3·5 to 6·3 V. At another site in this same monkey, both flexor digitorum longus and gastrocnemius gave larger EMGs with 33/sec. stimulation than with 83/sec. whereas biceps brachii (this was a site in the arm-leg overlap area) [4, 15] responded only to cortical stimulation at 83/sec. Thus, these frequency effects seem independent of stimulus intensity.

(3) *The interaction of the frequency effect with proprioceptive impulses.*—Amplitude and latency of the EMG resulting from stimulation of the motor cortex (Gellhorn [7, 8, 10]) and also in reflex experiments (Looffbourrow and Gellhorn [13]) are modified by proprioceptive impulses. This was shown by the fact that different initial positions greatly influence the responsiveness of various muscles to cortical stimulation. Even greater modifications were obtained by fixation of the joints at different angles. Fixation in extension increased the reactivity of the flexors and decreased that of the extensors while fixation in flexion had the opposite effect.

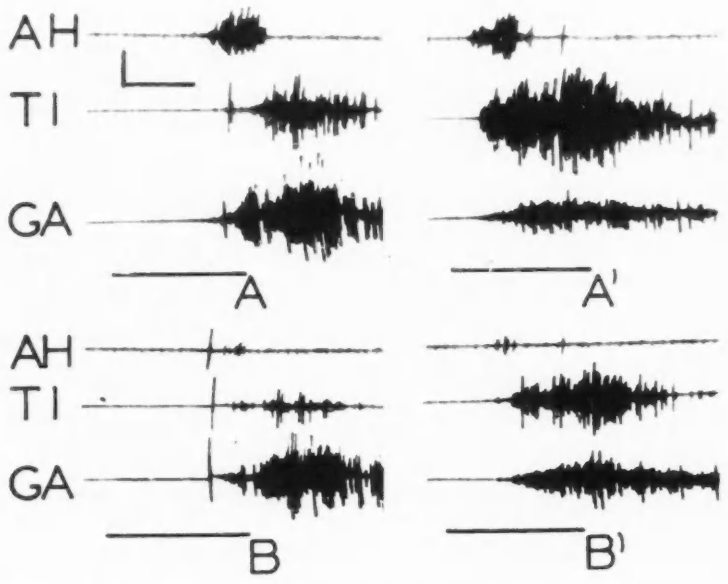

FIG. 5.—*Effect of ankle position and cortical stimulus frequency on EMG's.* Macacus rhesus. AH, adductor hallucis; TI, tibialis anticus; GA, gastrocnemius. Stimulation of site 12 (leg area, 4 mm. anterior to central sulcus) with 4·9 V. Hip fixated at 90 degrees, knee at 100 degrees in all experiments. A,A′ ankle 145 degrees. B,B′ ankle 65 degrees. A,B 33/sec. stimulation; A′,B′ 83/sec. Horizontal calibration 2 sec.

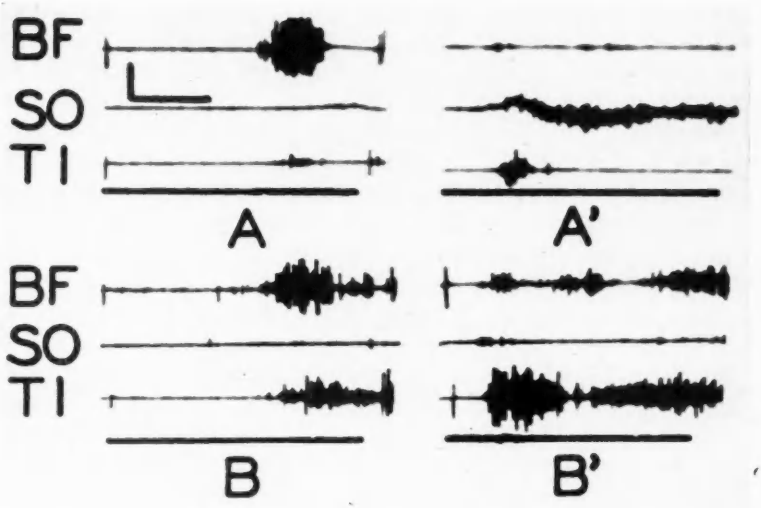

FIG. 6.—*Effect of leg position and stimulus frequency on EMG response.* Macacus rhesus. BF, biceps femoris (flexor part); SO, soleus; TI, tibialis anticus. Monopolar stimulation of site 12, 4 mm. lateral to mid-line, 4 mm. anterior to central sulcus, 3·5 V. Hip fixated at 90 degrees throughout. A,A′ knee and ankle 30 degrees; B,B′ knee 130 degrees and ankle 170 degrees. A,B at 27/sec.; A′,B′ at 83/sec. Horizontal calibration 2 sec.

These experiments raise the question as to whether the frequency effect would be altered through proprioceptive impulses.

The results are illustrated by figs. 5 and 6. In fig. 5 the limb was fixated, the upper records being during fixation of the ankle in plantar-flexion and the lower in dorsiflexion (the knee and hip being held in a neutral (90°) position throughout). Each of the recorded muscles can be seen to have responded with its largest EMGs not only in its own favourable proprioceptive condition but also its own optimal stimulus frequency, which for this cortical site was low for gastrocnemius and adductor hallucis (33/sec.) and high for tibialis (83/sec.). Thus, an appreciable response could be induced in adductor hallucis (AH) only with fixation of the ankle in plantar-flexion; in this position the EMG obtainable at 33/sec. was larger than that at 83/sec. The tibialis anticus response was also considerably increased with fixation in the proprioceptively favourable position of plantar-flexion, but 83/sec. stimulation of the cortical site induced a much larger response than 33/sec. in this muscle. The gastrocnemius record shows that the optimal frequency is independent of the type of joint fixation used. Fig. 5 shows again that latency and amplitude of response are independent phenomena.

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The EMGs reproduced in fig. 6, from a macaque, afford another example of the combined effect of proprioceptive position and cortical stimulus frequency on the pattern of response induced. Records of three hind-leg muscles biceps femoris (flexor part), soleus and tibialis anticus are shown, a cortical site of the hind-leg area being stimulated at 27/sec. and at 83/sec., with 3·5 V. The biceps femoris here responded with larger amplitude at a low stimulus frequency than at high; the other two muscles, however, showed a greater response to 83/sec. than to 27/sec. These frequency characteristics remained unchanged with the knee and ankle joints fixated at different angles. The largest tibialis EMG was obtained when the ankle was fixated in plantar-flexion (and the knee in extension) with the higher frequency of stimulation; soleus, conversely, responded primarily in dorsiflexion of the ankle (a favourable position for this muscle), but also mainly at the higher stimulus frequency (its responses in the other conditions being minimal). Similar results were obtained with forearm muscles tested in their reactions to cortical stimulation at different degrees of fixation and various frequencies.

Discussion

The chief result of this investigation is the establishment of the fact that the optimal frequency for a given muscle is different from various cortical foci and that muscles activated from the same cortical focus may have different frequency maxima. If the frequency maxima for agonist and antagonist are quite different the functional effect of cortical stimulation of a given focus must change with alteration in frequency. Indeed, it was seen in the non-fixated limb that the type of movement produced in response to cortical stimulation at one frequency would be a flexion of the toes and dorsiflexion of the ankle, while another frequency (higher or lower) applied to the same cortical site would result in the production of the opposite movement—extension of toes and plantar-flexion. Under conditions of fixation the alteration in the degree of innervation is indicated by the shift in the greatest magnitude of the EMGs from agonist to antagonist (cf. fig. 1). It speaks for the physiological significance of these findings that they were best obtained in lightly anæsthetized animals which showed some muscle tone and that in most instances minimal voltages were employed.

It seems reasonable to assume that as in experiments with artificial activation of the motor cortex by condenser discharges of varying frequencies the physiological processes underlying the voluntary activation of the motor cortex would lead likewise to impulses of varying frequencies depending on the intensity of the primary excitatory process. The experiments of this paper suggest that a given degree of excitation (leading to

a certain frequency of discharge) may elicit different types of movements from different cortical foci located in the same subdivision of a somatotopical area. Also, changes in the rate of discharge arising from a focus of excitation in the motor cortex may lead not only to quantitative but also to qualitative changes in movements.

That frequencies of stimulation of afferent nerves may alter the reflex pattern has been observed quite often (cf. Gellhorn [6] for the older and Bernhard and Skoglund [2] for the recent literature). Whether these effects are related to changes in synaptic transmission (synaptic resonance) as Bernhard and Granit [3] suggest or are due to specific differences in the reactivity of cord neurons in response to the original excitatory process is not known. The fact that proprioceptive impulses which act primarily but not exclusively on the spinal cord (Gay and Gellhorn [5]) do not modify the frequency characteristics of the cortically activated neurons appears to favour the assumption that the frequency characteristics of cortical neurons vary greatly.

Earlier experiments [8] showed that under the influence of proprioceptive reinforcement summation time decreases and amplitude of the EMG increases on cortical stimulation. In contrast to these findings results are more variable when the action of cortical stimulation with varying frequencies is investigated. It was shown that the summation period declines regularly with increasing frequency of stimulation but this reduction in latency bears no constant relation to the amplitude of the response; thus, an altered frequency to a cortical site serves in this respect to separate the two phenomena of summation time and magnitude of EMG which are parallel in the case of proprioceptive recruitment.

The maximal amplitude of response is in many cases not sustained throughout the period of stimulation, especially at the higher frequencies when the summation time is brief (*see,* for example, fig. C′; or fig. 3). The brevity of response at higher frequencies compared with that at lower was noted also by McCulloch [14] who explains it on the basis of increased threshold of the cortical neurons. However, it should be added that different cortical neurons behave differently in this respect as the biceps and triceps records of fig. 1 show.

Finally attention is called to the fact that the validity of the principle of multiplicity of cortical representation is well illustrated in the records of this paper which were obtained under near threshold excitation (cf. also Gellhorn [9]).

Summary

Experiments are reported on the effect of electrical stimulation of the motor cortex with condenser discharges of frequencies varying between

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10 and 102/second at near threshold voltages and with constant duration of the impulses. The activity of multiple fore- and hind-leg muscles is recorded simultaneously by means of electromyograms. The results were as follows:

(1) The pattern of response to stimulation of a single cortical site, as determined by observation of the movement of the free extremity, and as recorded electromyographically, may be different when the site is stimulated at a low frequency (*ca.* 30/sec.) from that obtained at a higher frequency of stimulation (60 to 100/sec.).

(2) This difference in pattern may be evidenced as a shift from a flexor response to an extensor one and vice versa; other shifts among the muscles activated may result in different types of movement.

(3) Two or more muscles activated from one cortical focus may have different frequency optima.

(4) The stimulus frequency which is optimal for a particular muscle at one cortical site may not be (and indeed often is not) the optimal frequency for the same muscle at a different cortical site.

(5) A response of a muscle to cortical stimulation at an optimal frequency for that muscle at that site may be increased by placing the limb in a favourable position for proprioceptive facilitation. However, the frequency characteristics are not altered by proprioceptive impulses or alteration in the intensity of stimulation.

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THE RESTORATION OF MOTOR FUNCTION FOLLOWING HEMIPLEGIA IN MAN

BY

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Introduction

The disorder of movement so commonly seen in hemiplegia in man has seldom been studied intensively. After the earlier essays of Todd (1856), Bastian (1886), Bergmark (1909), and Walshe (1919, 1923, 1929), it has generally been assumed that the static condition described in every textbook was adequately understood. If variations were recognized, they were in terms of the extreme of spasticity or flaccidity, and their explanation was left to indecisive physiological investigations. Anatomical studies of such cases have been inconclusive (Aring, 1940).

Hemiplegia manifests a large number of variants, both in the different conditions in which it occurs and at different times in the same patient. The present study is chiefly concerned with the course of recovery of movement following cerebral hemiplegia in an attempt to delineate some of the factors concerned. 121 patients have been observed. With the exception of 3, all suffered from a hemiplegia caused by thrombosis or embolism of one of the cerebral blood vessels. In the exceptions the hemiplegia was presumably due to a hæmorrhagic infarct in one, in another an angioma (shown by cerebral angiography), and in the third a glioma of the mid-brain and thalamus. All patients who exhibited coma over a long period of time, evidence of intracerebral hæmorrhage with rupture into the ventricles, or a severe aphasia which persisted for over a week, in addition to hemiplegia have been excluded from this study because of the complicating factors involved.

It was possible to follow 25 patients from the time of admission to the hospital to a point where a comparatively stable condition was reached. At the time of admission, 13 of these could not move either limb, 4 could move only the lower limb, and 8 could make weak movements in both extremities. Periodical clinical examination of each patient and electromyographic studies were employed in this series. From clinical evidence

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the lesions were all situated in the cerebral hemisphere, and most were in the internal capsule or subcortical white matter. To date there have been no autopsies on the patients reported here, and therefore no exact anatomical localization of the lesions can be offered. However, this report is chiefly concerned with a remarkable uniformity in the steps of recovery in different cases. Since in many respects the condition of cerebral hemiplegia is subject to great variation, it has been necessary to analyse the frequency of such variations in some detail, in order to emphasize the operation of the more constant associations. The anatomical correlation of certain variants awaits a more detailed clinical and pathological study. Some slight degree of sensory defect was demonstrable in 87 of the 121 patients studied, but the presence or absence of such mild sensory disturbance was not associated with any constant difference in the course of recovery. The changes which we shall describe were the same whether the lesion was in the so-called "dominant" or "non-dominant" hemisphere.

General Course of Recovery

Our first object was to establish the mode of recovery of ability to grasp a designated object with the affected hand, and for this reason we were chiefly concerned with the events in the course of recovery in the upper limb. Early in the study we observed 5 patients in whom there was finally a complete restoration of motor function in an upper extremity which previously had been completely paralysed. All movements in these extremities could be voluntarily executed as rapidly and as dexterously as those in the uninvolved limbs. The restoration of motor function in these cases followed a general pattern in which certain phenomena predominated during distinct phases or stages of the recovery process. It soon became clear that the evolution of recovery in those patients in whom restoration of motor function was not complete also followed the same general pattern, exhibiting all of the reactions of the recovery process up to a point where recovery halted. Each of the patients whom we could only observe for shorter periods of time could be fitted into one or more stages of this general pattern of motor recovery. Data obtained from some of these "short-term" patients will be used to illustrate special features of motor recovery.

Since the description of a series of special aspects of the process of recovery necessarily obscures the general course of recovery, we may here summarize the main course of events. Immediately following the onset of hemiplegia there was total loss of voluntary movement in the involved extremities, and a loss or diminution of the tendon reflexes. Resistance to passive movement was decreased in the involved extremities, but was seldom so complete as to be called flaccidity. Within forty-eight hours

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the tendon reflexes (excluding the finger-jerks) became more active in the paralysed extremities than in the uninvolved side, but were not clonic. In most of the patients the finger-jerks also became hyperactive within forty-eight hours, but in about a third of the patients this did not occur until three to twenty-nine days after the onset of hemiplegia. Within a short time a minimal degree of increased resistance to passive movement of the extremities began to appear first in the palmar flexors of the wrist and fingers and in the plantar flexors of the ankle.[1]

The resistance gradually increased in intensity and involved other muscle groups, so that the adductors and flexors were chiefly concerned in the upper extremity, and the adductors and extensors in the lower. Concurrently the tendon reflexes became brisker and clonus appeared one to thirty-eight days after the onset of hemiplegia, and one to thirty days after the first evidence of spasticity. Clonus was first seen in the plantar flexors of the ankle and involved these muscles frequently, although not infrequently the knee extensors and the palmar flexors of the wrist and fingers also exhibited clonus. The clasp-knife phenomenon appeared within three to thirty-one days after the onset of hemiplegia, and one to twenty-five days after the onset of spasticity, and involved the knee extensors and elbow flexors.

The first willed movements to return were a slight flexion of the shoulder and flexion of the hip, which appeared six to thirty-three days after the onset of hemiplegia. The ability to perform willed movement continued to improve so that eventually flexion of the elbow could also be accomplished, but not as a single movement. It accompanied flexion of the shoulder. Later palmar flexion of the wrist and fingers was added to this total flexion pattern in the upper extremity so that at first flexion of the fingers occurred as part of flexion of the upper extremity as a whole, that is, the shoulder, elbow, wrist and fingers simultaneously.

Even before this total voluntary flexion response developed, the patient could enforce a finger flexion obtained by certain proprioceptive stimuli. Thus if the observer delivered a series of finger-jerks or passive stretches of the tendons of the finger flexors, while the patient was simultaneously trying to flex his fingers voluntarily, the fingers flexed slowly but powerfully. Also, at this time the total flexor synergy could be facilitated by passive stretch of the corresponding muscles. At this time spasticity and

[1]In this paper the word flexion, with reference to any particular joint, refers to a movement which would withdraw the limb, and extension to a movement which would straighten the limb. Thus, flexion of the shoulder would be a movement which retracts the elbow. Movements of the digits of the foot and hand, and movements of the wrists and ankle are more difficult to classify in this way and for them we have retained the words plantar and palmar flexion and dorsiflexion.

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other signs of exaggerated proprioceptive reactions were at their height, and passive traction upon the flexor muscles of the arm could by itself cause active contraction of all the flexor muscles in the limb. This response, which we propose to call "proximal traction response," strongly facilitated the slow and feeble flexor synergy in the same muscles when the latter was the sole response to the effort of the patient. Both the total flexor synergy in the upper extremity in response to willed effort, and the proximal traction responses were facilitated or depressed by the tonic neck and body righting reflexes.

An extensor synergy of the arm, consisting of extension of the shoulder, elbow and wrist, and dorsiflexion of the fingers appeared soon after the earliest development of the flexor synergy. As in the case of the flexor synergy, the extensor synergy appeared first as a movement of the shoulder, with movements of the elbow, wrist, and fingers added later.

As the power of willed flexion of shoulders and elbow further increased, a stage was reached where spasticity in these muscle groups abruptly lessened. At the same time power of willed flexion of the fingers increased. Finger flexion could now be facilitated by a contactual stimulus moving distally across the palm of the hand. Movement of single digits became possible. Later a stationary contactual stimulus to the palm of the hand could also facilitate willed flexion of the fingers. As finger movements became more powerful and dexterous, spasticity abruptly lessened in the finger and wrist flexors and a well-defined grasp reflex could be obtained.

As mentioned previously, several patients recovered completely so that eventually they could execute any movement with the previously paralysed limb with the same degree of rapidity and dexterity as in the uninvolved extremity. Spasticity completely disappeared when complete recovery of the power of willed effort occurred. The tendon reflexes, however, remained slightly more active in the previously paretic limbs, but not clonic. An increased liability to fatigue and perhaps a very slight weakness in the previously paralysed limbs then remained as the only impairment of function.

The restoration of voluntary movement in the lower limb also began with the appearance of flexor and extensor synergies. As in the upper limb the flexor synergy appeared first, beginning as a flexion of the hip one to thirty-one days after the onset of hemiplegia. Flexion of the knee and dorsiflexion of the ankle were soon added to the hip flexion to make up the total flexor synergy. The appearance of an extensor synergy followed closely the development of the flexor synergy: it began with extension of the hip, with extension of the knee and plantar flexion of the ankle occurring sometime later.

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We have arbitrarily chosen to designate the recovery as complete when all movements of the limb could be performed with the rapidity and dexterity of similar movements of a limb which had not been paralysed. It must be emphasized that though the recovery process could be divided into "phases" or "stages" each of which could be maintained for a variable period, the recovery process was continuous and the gradual appearance of new factors resulted in overlapping of the different stages. Thus, the period of flaccidity immediately following the onset of hemiplegia was not abruptly followed by a period of exaggerated proprioceptive responses, but the tendon reflexes became more active while resistance to passive movement was not increased. Likewise, while proprioceptive reactions were still exaggerated, certain contactual effects appeared, and spasticity in various degrees could complicate the first voluntary movements.

Resting Posture

The resting posture of the paralysed limbs depended on the intensity of spasticity, and the influence of the tonic neck and body righting reflexes.

Of the 25 patients observed over a long period of time, all but 2 exhibited an abnormal resting posture at some time. Immediately following the onset of hemiplegia when the limbs were "flaccid" the posture depended upon passive placement of the limbs or upon gravity, but with the onset of spasticity, more constant postural abnormalities appeared. However, resistance to passive movement had to reach a certain intensity before abnormalities of posture resulted. In the 2 patients in whom no postural abnormalities were present, a very slight increase in resistance to passive movement could be demonstrated in the wrist and finger flexors, though this was never intense enough to produce an increased flexion of the fingers at rest. When postural abnormalities occurred, the first evidence of them was seen in the hand or foot, but without regular precedence in upper or lower limb. They were increased flexion of the fingers, and plantar flexion with slight inversion of the ankle.

9 patients showed increased flexion of the fingers as the only abnormality of resting posture during a long period until a stable condition had been reached or recovery had occurred. This abnormality occurred within forty-eight hours to ten days after the onset of hemiplegia. 4 patients showed increased flexion of the fingers together with plantar flexion and inversion of the ankle as the only postural abnormality during the entire period of observation. 2 patients developed a spastic posture of one limb. In 1 patient flexion of the fingers and plantar flexion of the ankle occurred within forty-eight hours of the onset of hemiplegia. Three days later a slight flexion of the wrist was detected. Without further change in the arm, spasticity in the hip adductors and extensors and knee

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extensors increased so that by the twenty-first day after the onset of hemiplegia the leg assumed a rigid, extensor posture. In the other patient no abnormality of resting posture was observed until twenty days after the onset of hemiplegia (this was also the first time any evidence of spasticity was detected) when the fingers were flexed and the ankle plantar flexed. On the thirty-first day after the onset of hemiplegia the wrist was flexed and by the fifty-second day the arm was slightly flexed at the elbow. No other postural abnormality was observed in this patient during a nine-month period when all neurological signs had stabilized.

8 patients developed the classical hemiplegic posture in both limbs. Flexion of the fingers and plantar flexion of the ankle were followed by increased flexion of the wrist and elbow, and extension of the hip and knee. Later the shoulder was found to be adducted and internally rotated, the arm flexed at the elbow, the wrist pronated (in 5 patients) or supinated (3 patients) and slightly flexed, and the fingers flexed. The leg was extended and adducted at the hip, extended at the knee, and plantar flexed at the ankle with slight inversion of the foot. No patient was observed with a flexion posture of the lower extremity or extensor posture of the upper extremity.

The time required to develop full hemiplegic posture varied considerably in the 8 cases. 4 patients showed the first postural abnormality within forty-eight hours following the onset of hemiplegia, while the others showed no abnormalities until twelve to twenty-four days following the onset of hemiplegia. 3 of them developed a total hemiplegic posture in five days; 2 patients did so in about four weeks, while the remaining 3 required from two to six months. In general, those patients who showed the first postural changes rather late after the onset of hemiplegia took the longest time to develop a complete hemiplegic posture.

In 97 patients whom we observed over shorter periods of time, postural abnormalities were not seen in all. Six exhibited a typical hemiplegic posture with flexed arm and extended leg as described above, 7 exhibited a flexed arm without any postural abnormality in the leg, 2 exhibited extension of the leg without any abnormality in the arm, and 22 presented minor degrees of hemiplegic posture. The other 60 patients showed no abnormality of posture, but at the time of their last examination, most of these were just beginning to develop mild spasticity, and it is probable that some postural abnormalities would have been detected were it possible to follow these patients for a longer time.

The classical hemiplegic posture of flexion in the upper limb and extension in the lower was therefore uncommon in fully developed form. Flexion of the fingers and wrist and plantar flexion of the ankle are the most commonly found spastic postures. As the response to effort became

more precise, spasticity lessened, and the associated postural abnormalities eventually disappeared. The most persistent postural abnormality in the upper extremity was then an increased flexion of the wrist and fingers. This abnormality disappeared in forty-three to sixty days following the onset of hemiplegia. Abnormalities of resting posture persisted in the patients whose recovery was not complete.

Exaggeration of Proprioceptive Responses

Tendon reflexes.—In 25 patients observed over a long period of time, the tendon reflexes (excepting the finger-jerks) became more active in the paretic limbs within forty-eight hours following the onset of hemiplegia. In 5 of these the biceps and the knee jerks were less depressed than the other tendon reflexes, and became hyperactive sooner. In the other 20, however, all of the tendon reflexes were equally depressed and became hyperactive at the same time. In 18 of these patients the tendon reflexes became hyperactive concurrently with the earliest appearance of an increased resistance to passive stretch of the muscles, while in the other 7 patients hyperactivity of the tendon reflexes preceded the earliest appearance of an increased resistance by three to twenty days. The tendon reflexes were not markedly exaggerated at this time, for any increased activity was minimal at first, and only by carefully comparing each tendon reflex with its counterpart in the uninvolved limb could any difference be detected. Within four or five days the tendon reflexes (excluding the finger-jerks) were quite obviously more active in the hemiplegic limbs, each reflex being a single contraction of both greater speed and amplitude than normal. A double beat or true clonic jerk was not present at this time.

The finger-jerks, on the other hand, did not always become hyperactive as soon following the onset of hemiplegia compared with the finger-jerk on the non-paretic side (which were absent in 19 of 25 patients). Hyperactive finger-jerks could be elicited within forty-eight hours following the onset of hemiplegia in 14 of the 25 patients. In the remaining patients a period of three to twenty-nine days elapsed before hyperactivity of the finger-jerks appeared, being preceded by some evidence of increased resistance to passive movement in 8. In the remaining cases, hyperactivity of finger-jerks appeared concurrently with the first evidence of increased resistance to passive movement. At this stage the finger-jerks were a quick, single jerk, and were never clonic.

A typical Hoffmann response, elicited in the usual manner by "flicking" the nail of the middle finger, was obtained in 16 of the 25 long-term patients. In 10 of these patients it could be elicited on the same day that the finger-jerks were found to be hyperactive. In the others

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a period of one to twenty-four days intervened between the earliest appearance of hyperactive finger-jerks and the Hoffmann response. The finger-jerks were not necessarily clonic when the Hoffmann response appeared.

Resistance to passive movement.—The resistance of the muscles to passive movement varied both qualitatively and quantitatively from individual to individual. It also varied during different phases of the recovery process and under the influence of the tonic neck reflex, body righting reflex, and the proximal traction response.

Following the period of "flaccidity" some increased resistance to passive movement was usually detected within forty-eight hours after the onset of the hemiplegia. However, in 6 of the 25 patients observed over a long period the first evidence of increased resistance presented on the third, fifth, ninth, seventeenth, eighteenth, and twentieth days respectively, and all eventually showed some increased resistance to passive movement.

Increased resistance to passive stretch did not appear abruptly. Its onset could not be demonstrated by shaking the limb passively, but only by inspection and palpation while the muscle was being stretched, and by comparing its resistance with that of its fellow of the opposite, normal, limb. In this way the initial appearance of resistance to stretch could be detected before the usually accepted signs of spasticity had appeared.

At its earliest onset, any increased resistance could be demonstrated only by stretch of the muscle through its full range. Thus, for example, it was necessary to extend the wrist beyond 180 degrees in order to demonstrate any increased resistance in the wrist flexors, and the resistance when encountered was very slight, having a soft and yielding character.

The increased resistance usually developed first in the flexors of the wrist and fingers and the plantar flexors of the ankle (15 of the 25 patients), but in 1 patient it first appeared in the flexors of the elbow. Gradually, after a further one to seventeen days all the flexors of the upper limb and extensors and adductors of the lower limb offered similar resistance. In the remaining 9 patients the onset was so rapid that when its appearance was first noted, it was present in all these muscle groups. 4 patients followed for a long period eventually exhibited an increased resistance to passive movement in the adductors and retractors of the shoulder, the flexors, and (with less intensity) the extensors of the elbow, the pronators and flexors of the wrist, and the flexors of the fingers. In the lower extremity an increased resistance was present in the extensors and adductors of the hips, the extensors of the knee, the plantar flexors of the ankle, and (with less intensity) in the flexors of the knee and hip.

3 patients exhibited an increase in resistance as described above except that the wrist supinators showed an increased resistance to passive movement rather than the pronators. More commonly the muscle groups in each extremity exhibited the pattern described above, except for absence of resistance in the shoulder and hip musculature. In many of these, and some others, the extensors of elbow and flexors of knee were not involved.

In spite of these variations in distribution of increased resistance, it was evident that the elbow flexors were involved three times as frequently as the shoulder muscles, and the wrist and finger flexors four times as frequently. In the leg, the knee extensors and ankle plantar flexors were involved twice as frequently as the hip groups.

In the larger group of patients who were observed for shorter periods, this distribution of spasticity was also observed. In addition 7 patients exhibited some increased resistance in the shoulder extensors, and 7 showed an increase in resistance in the shoulder abductors. The elbow extensors, as well as the flexors, showed increased resistance in 23. Increased resistance in the wrist and finger dorsiflexors was seen in 7 and 4 patients respectively and in the supinators in 2. Increased resistance was present in the flexors of the hip in 4, the knee flexors in 20, and in the ankle dorsiflexors in 3.

The intensity of resistance to passive movement was in general greatest in those muscles in which it first appeared. Of the whole group of patients examined, 6 cases showed a variation in this distribution of intensity. In 4 resistance to passive movement was more pronounced in the proximal groups of the upper limb, and in 2 it was more pronounced in the proximal muscles of the lower limb. In 4 of these 6 patients this distribution of intensity persisted, while in the other two this distribution changed so that within five to ten days the resistance was greater in the distal parts than in the proximal.

At its very onset the resistance to passive movement was difficult to demonstrate, and at this stage may be called slight. Yet within five to ten days, the resistance to passive movement was very obvious and easy to demonstrate, and sufficient to affect the resting posture of the joint. One might speak of such degree of resistance as being "moderate" in intensity. More usually a slight degree of resistance progressively increased to reach an intermediate "mild" degree within one to ten days. In 8 cases the resistance to passive movement could actually be considered "intense," and the early development of contractures was noted in this group. Occasionally the intensity of resistance could vary from mild to moderate and back again in the same muscle groups in day-to-day examination. This type of variation was rare, however. The changes

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in the intensity of resistance under the influence of the tonic neck reflex, body-righting reflex, proximal traction response, and during attempted voluntary movement were in contrast relatively constant.

Both the flexors and extensors acting on a joint presented an increased resistance to passive movement in a number of cases. In most of these the intensity of resistance was greater in the flexors of the arm, and extensors of the leg. In 5 cases the resistance in agonists and antagonists was seemingly equal, though the hemiplegic posture persisted. In 2 patients when lying supine an apparently equal degree of resistance was encountered in the flexors and extensors of the knee, and by the operation of the lengthening and shortening reactions the leg might be flexed or extended depending on the position in which it had previously been placed. In no case was the flexor resistance so great that the leg remained continually in an attitude of flexion, or the arm in extension.

The quality of increased resistance to passive stretch also varied. In the great majority of cases it was of a type having the generally recognized qualities of spasticity. While the muscle under examination was passively stretched, after a range of stretch during which no appreciable resistance was encountered, there occurred a progressive though slight increase in resistance. This resistance appeared more suddenly and was more pronounced, if passive stretch was carried out rapidly. When passive stretch was carried out resistance gradually increased in intensity, finally reaching a maximum, and then melted away rapidly before the end of the range of passive stretch. With the passage of time and further heightening of the stretch reflex, the range of passive movement before resistance was encountered became less, and the intensity of resistance became greater.

10 of the long-term patients developed a degree of abruptness of appearance and of melting of resistance, such as to be classified as a true clasp-knife phenomenon. 5 patients presented a clasp-knife phenomenon only in the knee extensors. The other 5 patients showed a clasp-knife phenomenon in both the knee extensors and the elbow flexors. The clasp-knife phenomenon appeared in three to thirty-one days after the earliest appearance of spasticity. In general, it appeared one to eight days after the onset of spasticity in the muscles concerned. No correlation was found between the intensity or quality of spasticity and the development of the clasp-knife phenomenon or clonus. In about half of the patients showing both of these phenomena, the resistance to passive movement was quite mild, while in the other half the resistance was moderate to intense.

In 3 patients, instead of the usual type of resistance which rose to a maximum toward the end of passive stretch and then melted quickly,

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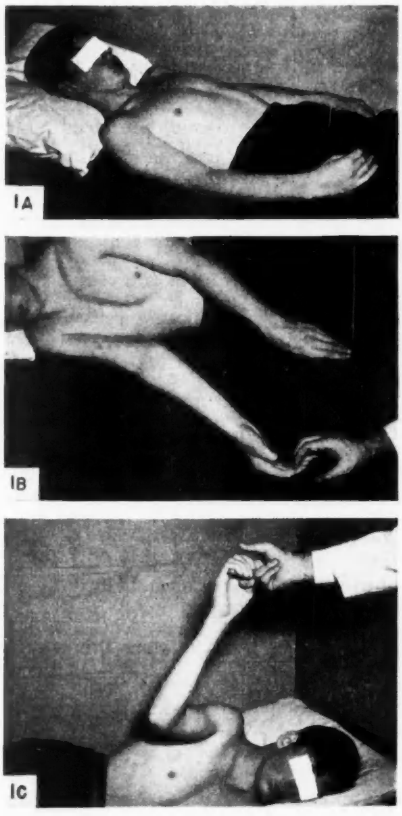

FIG. 1.—Photograph of patient R. B. with right hemiplegia, A, position of right arm with patient in supine position, B, attempt at elicitation of proximal traction response with patient lying on his right side. Flexion of fingers is no more than that occurring with the patient in the supine position, C, elicitation of the proximal traction response with the patient lying on his left side.

there was a resistance which rose to a maximum somewhat sooner before the end of passive stretch and faded away then more gradually. In 1 of these patients this type of resistance was present in the flexors of the elbow, wrist and fingers while the muscles of the leg presented the more usual type of resistance described previously. In the other 2 this variation was encountered only in the elbow flexors. In none of these patients was there any change in this quality of resistance during the period of observation.

In 2 patients another variation was observed. Here as stretch was continued after the onset of resistance, the resistance remained of the same intensity throughout the range of passive stretch and then melted rapidly

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at the end of passive movement. This was observed only in the elbow flexors while the resistance in other muscles was of the more usual type.

The resistance of the muscle did not always melt completely if stretch continued. In three cases a "plastic" type of resistance resembling the rigidity of extrapyramidal disease was encountered. Here increased resistance appeared after the beginning of passive stretch, allowing freedom for only about 10 degrees of the range of passive movement. The resistance then continued with about the same intensity throughout the further range of passive movement and without fading away at the end. This form of resistance was most apparent at the elbow where both the flexors and the extensors presented this same quality of resistance.

14 of the long-term patients eventually developed clonic tendon reflexes. 5 of these patients showed only clonic ankle-jerks, 4 had clonic knee and ankle-jerks, 3 had clonic finger and ankle-jerks, 2 had clonic finger, wrist, knee and ankle-jerks, and 1 had only a clonic knee-jerk. Clonic reflexes were not obtained elsewhere in these patients or in the other patients, although occasionally a double beat might be elicited in the biceps or triceps jerk.

In 5 patients clonic ankle-jerks were obtained forty-eight hours following the onset of hemiplegia. It is to be noted that clonic ankle-jerks were not obtained on the non-paretic side. In other patients clonic reflexes were obtained one to thirty-eight days after the onset of hemiplegia, and one to thirty days after the earliest appearance of spasticity. In general, clonic tendon reflexes reached their maximum seven to twenty days after the earliest appearance of spasticity in the muscles concerned in those tendon reflexes. In those patients who developed sustained clonus, it could be elicited within a day or two after the appearance of clonic tendon reflexes. A short time before a sustained clonus could be elicited, a clonic tremor could be felt superimposed upon the steadily increasing resistance to passive movement thus resembling the "cog-wheeling" of Parkinsonism. This phenomenon could not always be elicited, and rapid passive stretching of the muscle was most effective in eliciting it.

In 5 patients in whom voluntary movement was ultimately restored completely in the upper extremity, the intensity of spasticity increased parallel with the developing exaggeration of the proprioceptive reactions and decreased with the restoration of the power of willed movement. Spasticity was first noticed in these patients one to nine days after the onset of hemiplegia. In 1 of these patients, spasticity was found only in the wrist and finger reflexors, while in the other 4 it occurred in the elbow, wrist and finger flexors, and wrist pronators. In these patients, spasticity was never intense, being only moderate at its most pronounced stage. Spasticity reached its maximum intensity in from eight to twenty-one

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days. One of these patients developed clonic finger-jerks. The other did not develop clonic tendon reflexes, although all of the reflexes were markedly hyperactive. 2 patients developed a clasp-knife phenomenon in the elbow flexors. As power of voluntary movement increased, spasticity abruptly lessened, first in the shoulder and elbow flexors and later in the wrist and finger flexors. With complete recovery of motor ability no evidence of spasticity could be detected.

Restitution of Movement in Response to Willed Movement

Recovery from hemiplegia has been stated by many to occur first and be most complete in the proximal muscles of each limb, while willed movements of the hand and foot return last, are weaker, and are much more severely affected as far as dexterity of movement is concerned.

In our series of 25 patients followed throughout their course 13 could move neither arm nor leg, and 4 were completely paralysed only in the arm, at the time of admission to hospital. Of the 13 patients, 8 recovered some movement in both the arm and leg, 1 recovered movement in the arm only, 1 recovered movement in the leg only, and 3 did not recover any willed movement whatsoever. Of the 4 patients with only a paralysis of the arm, 3 recovered some movement of the arm, and 1 did not. The other 8 patients retained some power of willed movement from the onset, and their course could be fitted into the recovery process at a later stage. 2 of these patients could not perform any willed movement of the hand, however. All of our patients followed the general pattern of recovery, except that in 3 patients recovery followed the reverse order in the upper limb, for the ability to perform willed movement returned first in the hand, and later in the shoulder. The recovery of movement in the leg, however, followed the usual pattern in all our patients.

The first evidence of ability to perform willed movement in the upper limb was observed within six to thirty-three days following the onset of hemiplegia. This movement was a flexion of the upper arm at the shoulder, with exceedingly slow onset, limited range and power. One to six days later an associated flexion of the elbow occurred. This flexion of the elbow could not be performed separately. At this time the range of movement was extremely limited, and the power was only sufficient to overcome the force of gravity.

The ability to flex the fingers and wrist in response to willed effort occurred one to thirteen days after the development of the shoulder-elbow synergy, and six to forty-six days following the onset of hemiplegia. The ability to flex the fingers and wrist in response to willed effort, could only be performed as an addition to the shoulder-elbow flexion synergy. At the shoulder a slight adduction and internal rotation of the upper arm were

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now associated with the flexion. Therefore, the first stage in the evolution of ability to flex the fingers by willed effort resulted only in this flexor synergy of the arm, consisting of a flexion of shoulder (associated with a slight adduction and internal rotation) and flexion of the elbow, wrist, and fingers. At this stage the patient was totally incapable of performing any individual part of this movement separately, and any attempt to do so merely resulted in the execution of the total flexor synergy.

While these first movement patterns were appearing, a latent period of two to five seconds existed between the time the command to execute a movement was given and the time the actual movement took place. As the movement began it was very slow, but the speed increased toward the end of its limited range (fig. 2). Likewise, after the movement had been

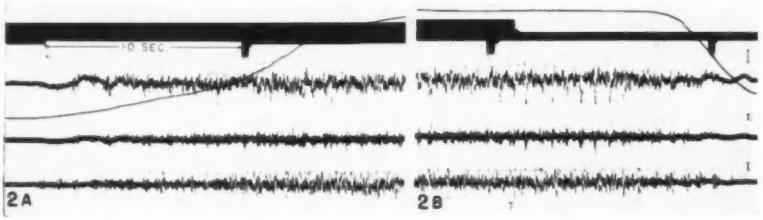

FIG. 2.—Electromyographic tracing from patient M. C. to show characteristics of the early return of the response to willed effort alone. Notches in the upper line of the tracing indicate time intervals of one second as shown. The line between the upper and middle galvanometer tracing is a balloon myograph record of muscular contraction of the flexors of the fingers. A command to flex the fingers was given one and a half seconds before fig. 2A and a time of one second separates fig. 2A and fig. 2B. At T in 2B the command to cease flexion was given. The two upper electromyograms are from m. flexor profundus digitorum. The lower electromyogram is from m. flexor sublimis digitorum. Calibrations to the right of 2B are for 100 microvolts.

executed and the patient was told to relax, relaxation did not take place immediately, but required one to three seconds to do so. It was also noted that immediately after the patient was told to cease voluntary contraction, the resistance in the contracting muscles was more intense than that present before voluntary contraction, and the tendon reflexes were more active than before voluntary contraction. This increase in the resistance and activity of the tendon reflexes also lasted for one to three seconds.

4 patients still exhibited the ability to produce this flexor synergy as the only recovery of willed movement in the upper extremity after periods of observation up to one and a half years. In these patients isolated movements at any joint could not be effected, nor did an extensor synergy of the arm ever develop. In the other patients further recovery occurred. As the flexor synergy of the arm appeared, an extensor synergy also

developed. The first movement to return at any joint was always a flexor movement, yet extensor movements could occur in the upper extremity before the ability to perform the total flexor synergy. Extensor movements could be made in the shoulder and elbow by the time the flexor synergy included the wrist and fingers. In 2 patients after willed flexion of the shoulder could be effected and before flexion of the elbow had returned, a weak extension of the upper arm at the shoulder could be made. Later extension of the elbow was added to this shoulder extension so that these two movements occurred together. Later, the extensor synergy consisted of extension with slight adduction of the shoulder, extension of the elbow and palmar flexion of the fingers. Dorsiflexion of the fingers began to occur some time later. Development of the total extensor synergy of the arm followed closely (within forty-eight hours) the development of the total flexor synergy.

In the leg, the return of voluntary movement followed the same general pattern seen in the arm. Movement returned first at the hip to be followed later by movement of the more distal parts, and flexor movements returned before movement of extension.

In 9 patients in whom the leg was completely paralysed at the onset of hemiplegia, and who recovered voluntary movement, willed flexion of the hip returned in one to thirty-one days. Willed flexion of the knee occurred within a day or two after the hip movement, except in 1 patient in whom willed flexion at the knee did not occur until twenty days had elapsed. At this time flexion of the knee could not be executed alone, and attempt to do so merely resulted in a combined flexion at the hip and knee as a flexor synergy of the lower limb. With the return of voluntary flexion of the knee, voluntary adduction of the hip could also be accomplished.

A complete flexor synergy of the leg became possible in these patients twenty-five days to three months from the onset of hemiplegia. It consisted of a flexion and adduction of the hip, flexion of the knee, and dorsiflexion of the ankle and toes. As this flexor synergy was appearing in the leg, an extensor synergy was also forming. Thus at a time when flexion of the hip and knee could be effected by willed effort, extension at the hip became possible. As in the arm, formation of the extensor synergy lagged behind the formation of the flexor synergy. The extensor synergy in its complete form consisted of an extension and adduction of the hip, extension of the knee, and plantar flexion of the ankle and toes. And, as in the arm, these synergies in the leg had a moderately long latent period of from two to five seconds from the time the command to move had been given and the time actual willed movement occurred. The individual movements comprising the synergy could not be performed separately.

As recovery progressed the latent period before voluntary movement

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shortened, the range of movement increased, and the power of movement became greater. In the arm pronation and supination were added to the flexor and extensor synergies. In all but 2 patients pronation of the hand accompanied both the flexor and extensor synergy. In these 2 patients, supination accompanied the flexor synergy, and pronation accompanied the extensor synergy.

The ability to flex either the wrist, fingers or elbow alone, without evoking the total movement synergy, returned gradually as power of willed movement increased. When the patient was first able to perform some individual movement (e.g. flexion of all the fingers, or flexion of the elbow) the remainder of the synergy was still difficult to suppress. Thus if the patient was asked to flex the elbow, and could actually perform this movement, some slight contraction of the flexor groups of the shoulder occurred also. Likewise, when the ability to flex all the fingers without flexing proximal joints first returned, this flexion was often associated with some contraction of the wrist and elbow flexors. This same difficulty also persisted in the lower limb. Spasticity could be quite intense even at the time the ability to perform these isolated movements returned, but as power of movement at the shoulder and elbow became comparable to that of the uninvolved shoulder and elbow, spasticity suddenly lessened, although it did not then disappear completely. In patients in whom a considerable degree of recovery took place, with increasing power of movement, spasticity abruptly lessened in the distal segments also, and at this time isolated movements of these segments could be performed without evoking even a fragmentary movement synergy.

3 patients exhibited a restoration of movement in the arm in a manner opposite to that just described. That is, willed movement returned first in the hand while movement of the elbow and shoulder returned later. The first response to willed effort in these patients was a weak flexion of all the fingers. This movement was followed in about five days by an associated flexion of the wrist and elbow which accompanied the finger flexion. Thus a flexor synergy formed in reverse order. At this time the power of contraction of the wrist and elbow flexors was less than that of the finger flexors. And at the time the wrist and elbow flexion occurred, some willed extension of the fingers could also be affected. After three to six more days flexion of the shoulder was added, completing the formation of the flexor synergy of the arm. The extensor synergy of the arm also developed, but lagged slightly behind the formation of this flexor synergy. The power of muscular contraction also developed in reverse order in these cases, being greater in the hand and wrist than in the shoulder. The ability to perform movements in an isolated fashion without evoking the total movement synergy also occurred first in the

fingers in these cases. In 1 of these patients before any movement of the shoulder could be obtained by willed effort, the spasticity of the finger, wrist and elbow flexors abruptly lessened with an increasing power of movement. In this patient isolated movements such as flexion and extension of the fingers and opposition of the thumb to each finger could be performed even before any willed movement at the shoulder was possible. The ability to perform shoulder movements which finally did return was not accompanied by any movement synergy in this patient. Some peculiarity of the lesion in these 3 patients evidently greatly shortened the process of recovery in the distal parts.

The movement defect in the arm in the presence of mild or moderate spasticity was studied in the 5 patients in whom recovery was complete and in 8 patients who were not completely paralysed at the time of admission to the hospital. We employed several simple tests to determine the dexterity of movement. These were alternating flexion and extension of the elbow, alternating pronation and supination of the wrist, finger-nose test, alternating flexion and extension of the wrist, flexion and extension of the fingers, and the ability to oppose the thumb to each finger from the index finger to the little finger and back again. All of these tests were carried out as rapidly as possible. The long latency which existed at the time of the flexor and extensor synergies were appearing thereafter steadily decreased. Some obvious latency might still remain, however, even when isolated movements could be performed. Thus, when attempting alternating flexion and extension of the elbow, the patient might show a latency (certainly not over one second) between each flexion and extension movement. As recovery progressed this latency rapidly lessened. Weakness was a major defect in the presence of spasticity, and was associated with rapid fatigue. Extension lagged behind flexion in the recovery process in all these respects, and this was especially apparent in the fingers.

In spite of a considerable return of power, the deficit in movement in the presence of spasticity was still striking. The more simple movements such as alternating flexion and extension, or pronation and supination, were performed more slowly than normal and appeared stiff and awkward. Occasionally the smooth flow from flexion to extension would cease at one point, the limb remaining flexed or extended for more than one second before executing the reverse component. On finger-nose testing or even simple alternating flexion and extension at the elbow, a clonic tremor at the elbows developed in 2 patients.

The disorder of willed movement in the presence of spasticity was most clearly demonstrated in the fingers. When the ability to flex and extend the fingers without evoking the total movement synergy of the arm

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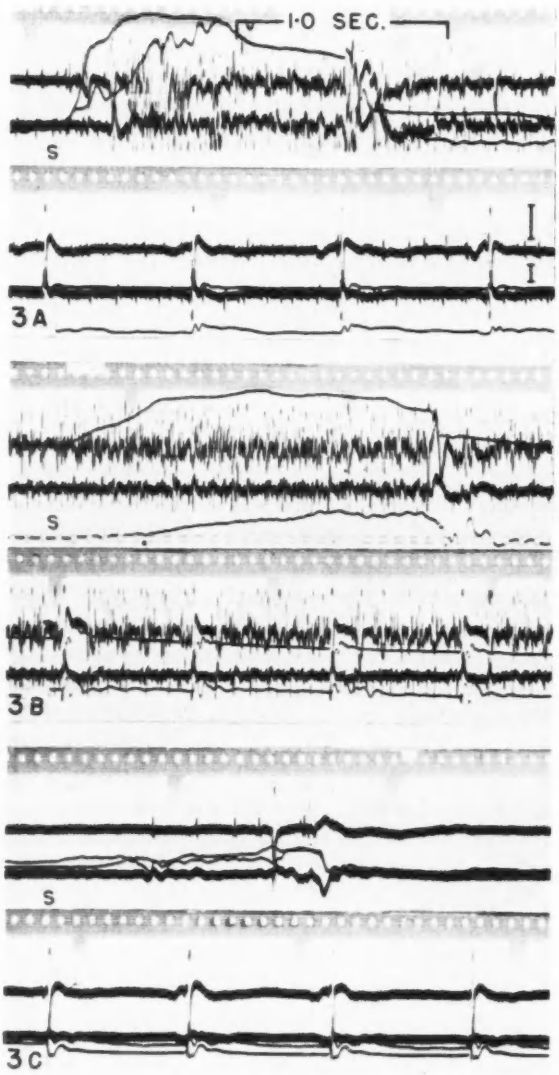

FIG. 3.—Electromyographic tracing from G. A. with right hemiplegia. The galvanometer tracings are accompanied by two black lines, the upper being a recording of the pressure exerted by the stimulus, and the lower being a myographic tracing for the flexors of the fingers. The upper EMG is from m. flexor digitorum profundus, and the lower from m. flexor digitorum sublimis. Upper record for each series, is of response to passive stretch, lower record of tendon jerks over a stretch reflex background. Stimulus at S. Calibration at 100 microvolts.

FIG. 3A.—Patient in supine position. FIG. 3B.—Patient on left side.
FIG. 3C.—Patient on right side.

occurred, isolated movements of each finger still could not be performed. Thus, if the patient was instructed to move the index finger, or the little finger alone, any attempt to do so caused either flexion or extension of all the fingers. At this stage the fingers could not be closed completely, most of the movements occurred in the joints of the phalanges, and very little movement occurred at the metacarpophalangeal joint. If the patient was instructed to make a fist, the thumb did not close around the flexed fingers, but remained slightly extended.

The ability to flex or extend one finger separately returned first in the index finger. The middle and little fingers were next to acquire this ability, though at first there was a flexion or extension of the ring finger associated with a flexion or extension of the little finger. In later recovery this associated movement disappeared. In one patient flexion of the little finger caused an associated slight flexion of the middle and ring fingers and a rapid hyperextension of the index finger. This association also vanished with the full recovery of dexterity in this patient.

When opposition of the thumb and digits could first be performed, the thumb could only be exposed to the index finger. As recovery progressed, the thumb could be opposed to more and more fingers until finally it could be opposed to any. When opposition to all fingers was first possible, several movement defects were still apparent. First, in opposing to the fingers, the thumb did not flex in the natural manner, but remained partially extended. In early opposition of the thumb to each finger, most of the activity was carried out by the thumb, that is, the fingers flexed little, and the thumb was moved along from finger to finger. Flexion of the fingers to meet the thumb was mostly at the metacarpophalangeal joint, with very little flexion at the interphalangeal joints. Therefore, the thumb was not truly opposed to the tip of each finger. Occasionally the finger-thumb opposition test revealed tremors of the fingers or thumb while the test was being carried out, and with fatigue "contraction fasciculations" were not uncommon in the muscles concerned.

As recovery progressed these defects were less and less apparent, and movements became more rapid and more dexterous. All movements could be performed with greater speed and dexterity if the patient was allowed to watch his hand or limb. If vision was excluded, movements were carried out more slowly and with considerably less dexterity. Any wavering ataxia or tremor was increased by excluding vision even though no defect in sensation could be found by clinical testing. Such defects in movement still occurred in the presence of only slight or mild spasticity. Spasticity finally disappeared with complete recovery of speed or dexterity of movement. Not only were the tests mentioned above performed as quickly and as dexterously as with the normal limbs, but there was also

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an absence of difficulty in performing such tasks as writing, sewing, buttoning or unbottoning a shirt, or tying shoe-laces, with the eyes open or closed. The only defects then remaining were a very slightly diminished power and an increased liability to fatigue.

Proprioceptive Facilitation

During the period when proprioceptive responses were increasingly exaggerated, and before any muscular contraction could be made in response to willed effort, certain proprioceptive reactions and the willed effort to produce a movement could mutually facilitate each other. These effects could be most easily and effectively demonstrated for flexion of the fingers.

The mutual facilitation of proprioceptive reactions and willed effort could be demonstrated in the earliest phase of recovery of stretch and tendon reflexes. Indeed a willed effort could sometimes enable one to elicit a latent tendon reflex or other pathological sign. For example, in one patient the biceps, triceps and supinator reflexes had all become hyperactive within forty-eight hours following the onset of hemiplegia. Finger-jerks could not be elicited until the tenth day following the onset of hemiplegia. The arm was completely paralysed. However, on the eighth day, if the patient was instructed to attempt flexion of his fingers while the examiner simultaneously attempted to elicit finger-jerks, small, brisk finger-jerks were obtained. (Finger-jerks were elicited by resting the patient's fingers, palmar surface down, on the examiner's middle finger and tapping the examiner's finger with the reflex hammer.) If an attempt was made to elicit finger-jerks without the patient's willed effort to flex the fingers, no response occurred. Likewise, if the patient attempted to flex his fingers while the examiner was attempting to elicit a Hoffman sign (in the customary manner by flicking the finger nail of the patient's middle finger), a Hoffman response with flexion of all the fingers and thumb was obtained. Without the simultaneous willed effort of the patient, no responses could be obtained.

Within a day or two after these latent pathological signs were elicited by such willed facilitation, the same responses could be obtained without requiring the willed effort of the patient. However, at this time the feeble, small finger-jerks could be facilitated in amplitude and speed by the simultaneous willed effort to flex the fingers.

At a time when voluntary flexion of the fingers still failed, an attempted flexion of the fingers while the examiner delivered a series of taps to the lightly stretched fingers at the rate of two taps per second resulted in flexion of the fingers so as to close them almost completely. When this phenomenon first appeared the resulting contraction of the finger flexors

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was a jerky, irregular movement. As each finger-jerk was elicited (the willed effort to flex the fingers being applied continuously) the relaxation following each finger-jerk was greatly delayed. Thus the fingers closed by accumulation of the increased after-discharge of the repeated finger-jerks (figs. 4 and 5). The flexion which occurred with this facilitation began in

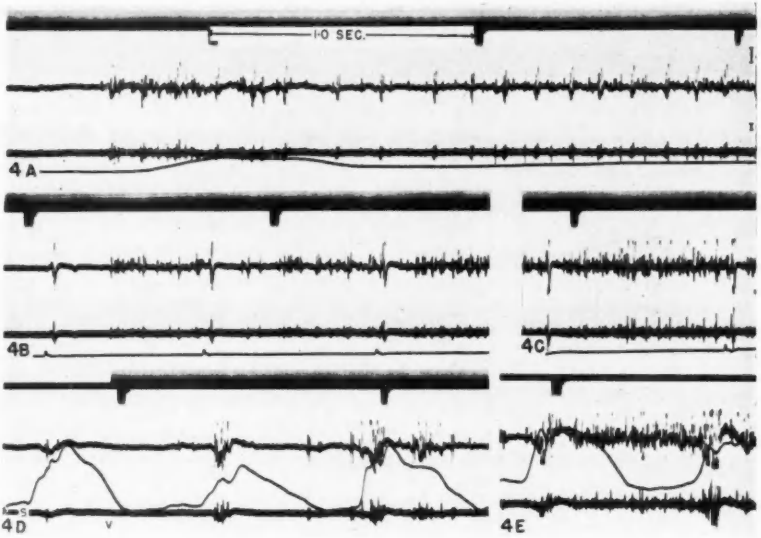

FIG. 4.—Electromyographic tracing of patient G. H. with right hemiplegia. Upper line for time intervals of one second. Both EMGs are from m. flexor digitorum profundus. Lower black line is tracing of balloon myograph over finger flexors. Calibration at 100 microvolts.

FIG. 4A.—Attempt at willed flexion of fingers alone.

FIG. 4B.—Willed flexion of fingers accompanied by repeated finger-jerks.

FIG. 4C.—Continuation of 4B after about four seconds.

FIG. 4D.—Willed flexion of fingers accompanied by repeated passive stretch applied to the finger flexors. S, signifies passive stretch of finger flexors. V, signifies command to begin willed flexion.

FIG. 4E.—Continuation of 4D after approximately five seconds.

the two distal phalanges; flexion at the metacarpophalangeal joints began after the fingers were half-closed. The facilitated flexion continued for several seconds after cessation of willed effort, and the resistance in the finger flexors was then greatly intensified over that previously present. This increased resistance persisted for one to five seconds. During this period the finger-jerks were found to be more brisk and of greater amplitude than before the facilitated flexion.

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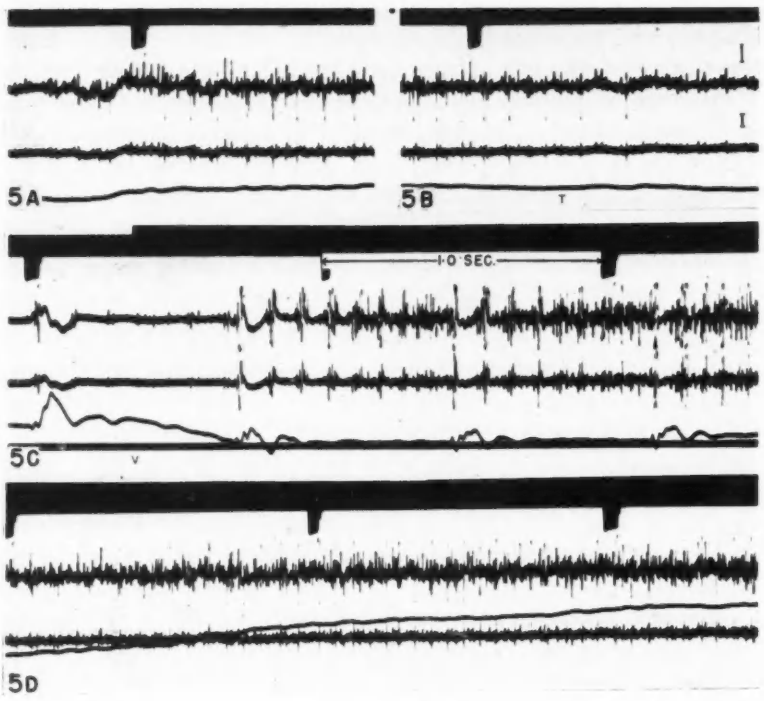

Fig. 5.—Electromyographic tracing from B. W. with left hemiplegia. Upper line time intervals of one second. Both EMGs from m. flexor digitorum sublimis. Lower black line for balloon myograph over flexor surface of index finger. Calibration at 500 microvolts.

Fig. 5A.—Attempt at voluntary flexion of fingers alone. The beginning of the attempt was quarter second before beginning of figure.

Fig. 5B.—Continuation of 5A, but one second later.

Fig. 5C.—Voluntary flexion with repeated finger-jerks. V marks beginning of voluntary effort.

Fig. 5D.—Voluntary flexion of fingers alone around three of the examiner's fingers. Note that the balloon myograph line rises higher in 5D than in 5A and 5B indicating an increased tension.

In 3 patients a latent period of four to five seconds existed between the time the command to flex the fingers was given and the facilitated flexion began. Gradual increase in the finger-jerks occurred towards the end of this period. These effects were obtained more rapidly within three to five days after the phenomenon was first noted. In the other patients the finger-jerks and increased flexion of the fingers took place immediately following the command to flex, during a series of finger taps. A single

tap on the tendons of the finger flexors was not sufficient to facilitate any willed effort. Active flexion of the fingers relaxed almost immediately when tapping on the fingers ceased, in spite of continued willed effort. With continued recovery this facilitation was easier to elicit, of shorter latency and increased power. Its jerky character became smoothed out so that finger flexion occurred as a sustained clonic contraction, of which the rhythm was determined by the finger-jerks used for facilitating the willed flexion.

With increasing facilitation other muscle groups beside the flexors of the fingers joined the response. If the patient attempted to pull against the fingers of the examiner while intermittent finger-jerks were being delivered, flexion not only occurred in the finger flexors but also in the flexors of the wrist, elbow, and shoulder. In 3 patients none of these additional movements could be performed by willed effort alone at this time, nor could the flexor synergy of the arm be executed by willed effort alone. In its full development proprioceptive facilitation had all the characteristics of the proximal traction response.

Proprioceptive facilitation presaged the return of ability to voluntarily flex the fingers by one to thirteen days, but did not always precede the earliest return of any voluntary movement in an arm. In 4 cases some voluntary flexion at the shoulder was possible before proprioceptive facilitation of finger flexion could be obtained. After the first ability to flex the fingers in response to command made its appearance, voluntary flexion accompanied by periodic tendon-jerks or by sustained traction against the fingers was more powerful and of greater range.

Other means of facilitating willed effort by proprioceptive stimuli were investigated. Passive hyperextension of the fingers, to set up a stretch reflex in the finger flexors, was found to be ineffective when proprioceptive facilitation first made its appearance. Within two days following the appearance of facilitation by tendon reflexes, some facilitation occurred with passive stretch of the finger flexors in 2 patients, before the ability to flex the fingers in response to willed effort alone had returned. The latent period of voluntary flexion was shortened less by passive hyperextension than by repeated tendon-jerks, and the flexion was not as complete in range or as powerful. Later, when some ability to contract the finger flexors in response to willed effort had returned, passive hyperextension of the flexors enabled a more powerful voluntary flexion. Repeated periodic passive extensions were more effective than one (figs. 4D and 4E).

Facilitation was also attempted by hyperextending only one finger, but this was the least effective method. It enabled only a stronger willed flexion of the finger extended and a very slight flexion of the distal phalanges of the finger on either side of the extended one. However,

after weak voluntary flexion of the fingers could be accomplished, this means of facilitation enabled the patient to flex all of his fingers more effectively than by willed effort alone, but never as completely or as powerfully as when stretch of all the fingers or finger-jerks were used for facilitation. It was, of course, necessary to stretch all the finger flexors slightly in order to elicit finger-jerks.

When these proprioceptive facilitating mechanisms first made their appearance, the reactions could be rapidly fatigued by several trials in succession. There was, however, no change in the amplitude or briskness of the finger-jerks or in the resistance to passive movement, both of which continued to become even more exaggerated. It was apparent that the willed part of the response was the seat of fatigue. Proprioceptive facilitation of finger flexion was obtained in 12 patients who were unable to flex the fingers in response to voluntary effort alone at that time. This facilitation followed the onset of hemiplegia by eight to forty-six days: it followed the first appearance of spasticity by one to forty-three days.

Facilitation by Righting Reflexes

Certain reactions caused a change in the resting posture, and in the intensity and distribution of spasticity in the hemiplegic limbs. Since passive turning of the patient's head by the examiner was usually ineffective in eliciting a tonic neck reflex, the response was usually elicited by having the patient voluntarily and forcefully turn his head to one side or the other. Such intensification of tonic neck reflexes was effective in 6 patients in whom the resistance to passive movement was quite marked in the flexors of the arm and extensors of the leg. In these patients, however, the change in the position of the head affected the arm only. In no case was any effect seen in the leg.

Only in one patient with moderate resistance present at all joints in the upper extremity, including the shoulder, was an actual change in posture of the hemiplegic arm observed. Thus when the patient forcefully turned his face as far as possible to the side of the hemiplegia there was an extension of the hemiplegic arm. The wrist pronated and dorsiflexed slightly and the fingers flexed in moderate degree. With the face turned away from the hemiplegic side, the arm flexed strongly at the elbow and adducted at the shoulder. The wrist supinated, and the fingers remained flexed. Resistance to passive movement underwent corresponding increase in the active muscles. In the other 5 patients, although no active change in the posture of the hemiplegic limbs occurred with turning of the head, a striking change took place in the intensity and distribution of resistance to passive stretch. Thus when these patients forcefully turned their faces to the hemiplegic side an increase in the resistance to passive

movement could be demonstrated in the extensor muscle groups, while the resistance in the flexor groups diminished. The diminution in resistance to passive stretch in the flexors resulted in its complete abolition in only one case. In the other cases the flexors always presented more than normal resistance, but not as much as the extensors. With the face turned away from the hemiplegic side, resistance to passive stretch increased in the flexors and decreased in the extensors. In 2 cases the resistance in the extensors disappeared completely.

The effect of body position on the posture and resistance to passive movement of the hemiplegic limbs was even more striking. With the patient lying in the supine position the upper limbs were flexed and the lower extended. If the patient turned on his side with the hemiplegic limbs uppermost, the flexion of the elbow, wrist and fingers was greatly increased. Likewise, there was great intensification of resistance to passive movement in the elbow, wrist and finger flexors, and to a lesser extent in the retractors and adductors of the shoulder. In one patient the leg also flexed at the hip and knee. In the other patients, however, any effect on the leg was best demonstrated by passive manipulation of the extremity, whereby an increased resistance could be shown in the flexor muscles and hip adductors. The diminution in extensor resistance was more evident, however. The tendon reflexes in the upper limb all became more brisk, with wider amplitude, and occasionally initiated clonus.

When the patient was on his side with the hemiplegic limbs lowermost, an extension of these limbs took place, including some extension of the fingers. The postural change was more evident in the arm than in the leg, although one patient showed active extension of the leg. There was now a pronounced redistribution of resistance in the various muscle groups, being greatly increased in the extensors and reduced in the flexors. Indeed in one case, all flexor resistance disappeared, but in the others slightly greater than normal resistance still remained. The tendon reflexes again exhibited a remarkable change. Instead of being clonic and of great amplitude, they were now small, rapid, single contractions. Indeed the finger-jerks were very feeble and difficult to elicit. The electromyographic features of this reaction from a patient studied also by Drs. Seyffarth and Denny-Brown (1948) are illustrated in fig. 3.

In work with Dr. Denny-Brown on pyramid lesions in the monkey, the author learned to recognize the characteristics of a righting reflex which was manifested as a facilitation of flexion of all joints in response to traction on the flexor and adductor muscles of the shoulder. If the traction was made by pulling on the fingers, this response must be distinguished from the grasp reflex, by excluding a moving tactile element

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from the stimulus, and by the strong associated flexion of wrist and elbow which is characteristic of it. When proprioceptive reactions were most highly exaggerated in human hemiplegia this response, which we propose to call the "proximal traction response," could also be obtained.

The response in the hemiplegic patient was a slowly developing, strong flexion of the shoulder, elbow and wrist which could be reinforced by various other reactions, and then included flexion of fingers. The reaction depended on stretch or traction applied to the flexor muscles of the limb, each of which reinforced the others. Thus although simple traction on the finger flexors themselves did not reveal anything more than an increased resistance to passive stretch, traction on the flexors of the fingers of sufficient force to cause also traction on the wrist and elbow flexors and through these traction on the shoulder muscles, was then followed by increased flexion of the fingers together with an associated increased flexion of the wrist and elbow. If the traction was made on the wrist or elbow flexors alone, and not on the finger flexors, with enough force to cause traction on the shoulder, flexion was intensified in the wrist and elbow flexors, or elbow flexors alone. However, when the reaction was prominent, the fingers also flexed with traction on the wrist flexors. With this method of elicitation it was clear that the response differed completely from the grasp reflex. This response fatigued easily, and renewed traction on the flexors involved was necessary to reinforce it.

The proximal traction response was reinforced to some extent by the operation of the tonic neck reflexes. Thus with the patient facing away from his hemiplegic limbs, the elicitation of the traction response resulted in a considerably more powerful flexion than that obtained with the patient facing forward. The effect of body posture on the proximal traction was response even more striking. With the patient lying on his side with the hemiplegic limbs lowermost, however, the response was abolished and could not be obtained by any stimulus or combination of stimuli (fig. 1B). When the hemiplegic limbs were uppermost the response was greatly intensified (fig. 1C).

When fully developed the proximal traction response could also facilitate movements in response to willed effort. Thus flexion of the fingers was greatly facilitated if, while the patient voluntarily flexed his fingers, the examiner exerted traction against the fingers causing secondary traction on the elbow and shoulder. The response then became a more powerful flexion at all these joints, and the flexor synergy resulted. Likewise, the ability to flex the limb by willed effort was facilitated by the tonic neck reflex and body righting reflex. The same process doubtless underlies the spread of facilitation with finger-jerks to affect a flexion not only of the fingers, but also of the wrist, elbow and shoulder.

The development of the traction response was followed in 12 patients. This response was first obtained when other types of proprioceptive facilitation were already present, and usually two or three days after the onset of localized proprioceptive facilitation. In 3 patients the traction response could not be obtained until five or six days after facilitation by tendon-jerks and simple stretch first occurred.

Contactual Facilitation and the Grasp Reflex

With the first return of willed flexion of all the fingers, this flexion could be facilitated by means other than the proprioceptive methods described above. Thus when willed flexion of the fingers was only a weak and incomplete movement (the patient being able to close his fingers only half-way, for example) a contactual stimulus to the palm of the patient's hand simultaneously with the patient's willed effort to flex his fingers led to a more powerful and complete flexion of the fingers. An effective contactual stimulation could be delivered in several ways. In the most simple methods the examiner used his fingers as the stimulating agent. Either the examiner stroked the palm of the patient's hand with his finger tips, moving in a distal direction out on to the palmar surface of the patient's fingers, or the examiner could draw his fingers across the patient's palm out between the thumb and index finger. The first method was the more effective. In order to demonstrate this effect it is important that the stimulus be light enough not to stretch the flexor tendons and so introduce an added factor of proprioceptive facilitation. With the first appearance of such contactual facilitation a stimulating agent of broad surface was necessary, and stimulation with an agent of small contacting surface, such as a pencil, was ineffective. At that stage it was also necessary to use a moving stimulus, stationary contact with the patient's palm being completely ineffective.

Such contactual facilitation, unlike proprioceptive effects, occurred only when some response to willed effort was already possible. Two to three days after its first appearance contactual facilitation became more effective and stationary contact alone could then facilitate willed flexion of the fingers. The stimulating agent still had to be of broad surface area, however. Thus, if the patient was told to close his fingers round the examiner's hand, which had been placed in the patient's palm, a more powerful and more complete flexion of the fingers resulted than if the patient attempted to flex his fingers without contact (fig. 5D). Like proprioceptive stimuli these contact stimuli could also reduce the latent period preceding the onset of voluntary flexion.

Contactual facilitation could be demonstrated in 10 patients of the

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long-term series, and occurred within eight to fifty-four days after the onset of hemiplegia.

The grasp reflex.—As movement of the shoulder and elbow became more powerful, spasticity abruptly lessened in the shoulder and elbow muscles. Likewise as movements of the wrist and fingers became more powerful and could be effected without development of the flexor synergy of the arm, spasticity in the wrist and finger flexors also suddenly lessened. At that time a contact stimulus alone could initiate a flexion of the fingers which was identical with the grasp reflex. Although the grasp reflex was obtained only with a decline of spasticity, the activity of the tendon reflexes could, nevertheless, continue to increase for a time. For example, in one patient, in whom a moderate spasticity of the wrist and finger flexors declined abruptly on the twenty-ninth day following the onset of hemiplegia, the grasp reflex was first elicited on that day. Within a few days the finger-jerks, which had previously been hyperactive but not clonic, were first shown to be clonic. The patient recovered completely in another thirty days and the clonic element by then had disappeared.

Seyffarth and Denny-Brown (1948) have defined the grasp reflex as "a stereotyped prehensile reaction of the flexors and the adductors of the fingers, and the flexor muscles of the wrist, which can be elicited in fractional parts by appropriate localization of the stimulus. The adequate stimulus for the full reaction is dual. The first essential is a distally moving deep pressure over a specific area of the palmar surface of joints in the hand, which elicits a rapid brief muscular contraction (the 'catching' phase), which develops into a strong 'holding' phase only if traction is made upon the tendons of the flexor or adductor muscles thus thrown into preliminary contraction. The response is then maintained only by traction."

In 5 of our patients the development and elaboration of the grasp reflex was studied. A grasp reflex of the elementary type described by Seyffarth and Denny-Brown, which requires a heavy pressing, moving contact for its elicitation, was first obtained twenty-three to forty days following the onset of hemiplegia, and preceded complete recovery, according to our criteria, by twenty to forty days (*see* Table I).

The ability of the patient to move the fingers was profoundly modified by the appearance of these contactual reactions. Prior to the appearance of contactual facilitation of willed movement first mentioned above, voluntary flexion of the fingers was very weak. The range of movement was extremely limited, the fingers being able to flex only 2 or 3 cm. Contactual facilitation itself enabled the fingers to flex completely, with considerable increase in power. Although contactual facilitation appeared

THE RESTORATION

TABLE I

	Finger-jerks	*Spasticity*	*Proprio facil.*	*Traction response*	*Vol. movt. hand*	*Tactile facil.*	*Grasp reflex*
Complete recovery							
G. H.	9 days	9 days	9 days	10 days	10 days	16 days	40 days
N. F.	48 hours	48 hours	8 days	13 days	15 days	15 days	23 days
*C. Y.	48 hours	48 hours	8 days	8 days	11 days	11 days	29 days
†K. B.	48 hours	48 hours	48 hours	48 hours	7 days	8 days	23 days
A. M.	6 days	48 hours	6 days	6 days	12 days	14 days	26 days
‡H. C.	48 hours	9 days	9 days	9 days	15 days	?	?
Recovery incomplete							
J. H.	18 days	18 days	18 days	18 days	23 days	26 days	0
M. C.	48 hours	48 hours	18 days	18 days	19 days	?	0
J. A.	48 hours	48 hours	15 days	15 days	25 days	26 days	0
Flexor synergy							
R. B.	20 days	20 days	31 days	36 days	43 days	46 days	0
W. W.	3 days	3 days	46 days	46 days	54 days	54 days	0
B. W.	48 hours	48 hours	25 days	31 days	38 days	39 days	0
E. D.	9 days	9 days	?	?	30 days	?	0
No recovery							
J. N.	6 days	5 days	0	0	0	0	0
W. M.	28 days	9 days	0	0	0	0	0
M. M.	3 days	48 hours	0	0	0	0	0
G. M.	7 days	48 hours	0	0	0	0	0
§M. M.	48 hours	48 hours	0	0	0	0	0
B. T.	48 hours	48 hours	0	0	0	0	0

*†These patients were able to move their upper limbs at the shoulder and elbow by effort of will alone at the time of admission. They could never execute willed movements of the wrist and fingers, however.

‡This patient died of pneumonia before the recovery process had halted. Because of the time-sequence of events in early recovery he is included under the group who recovered completely.

§This patient did recover the ability to flex the upper arm at the shoulder.

in these patients when willed effort produced only the flexor synergy, the movements at each joint could not be performed separately until after the appearance of contactual facilitation With the appearance of the grasp reflex, willed movement of the fingers was even more profoundly changed. Prior to the appearance of the grasp reflex, the finger movements were hindered by spasticity; they were slow and clumsy, and stiffness appeared to contribute largely to the defect. Isolated movements of the digits and opposition of the thumb and fingers, if present, were carried out only with the greatest difficulty. Attempts to move a finger alone often could not be accomplished, and any attempt to do so resulted in movement of all the fingers. Prior to the appearance of the grasp reflex, all of the defects described were made much worse if the patient was blindfolded so that he could not watch his fingers. This occurred even though no sensory defect could be demonstrated. After the appearance of the grasp reflex, finger

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movements were much more powerful and dexterous. Then slowness and clumsiness due to spasticity was greatly reduced. Speed of movement was greatly increased. Isolated movements of the fingers and finger-thumb opposition could be performed with relative ease.

The proximal traction response and the grasp reflex might be confused, but they are two entirely different reactions. The traction response was obtained when proprioceptive reactions were at their height. The grasp reflex on the other hand was only obtainable with a decline of spasticity. Stretch of the muscles concerned was not a primary factor in obtaining the grasp reflex. Indeed, the grasp reflex could be obtained with the wrist flexed to 90 degrees so that the flexor muscles were well relaxed and the element of stretch was eliminated. The fully developed grasp reflex involved flexion and adduction of the fingers and only secondarily a flexion of the wrist. The strong flexion at the wrist and elbow which was seen in the traction response did not occur in the grasp reflex. Finally, the grasp reflex was not influenced by the operation of the tonic neck and body righting reflexes.

Relationship of the Various Phenomena to Ultimate Recovery

19 patients were studied in detail with observations over a prolonged period, with special reference to the inter-relation of the various postural mechanisms and the recovery of voluntary movement. 17 of these patients could not move the arm at the time of admission. 2 could perform willed movements of the shoulder and elbow when first observed, but not of the wrist or fingers. At the end of the period of observation 5 of these patients recovered completely; 5 still could not move any part of the arm; one could only flex the shoulder; 4 could only execute the flexor synergy of the arm; and 3 recovered all movements of the arm, though spasticity and weakness remained to a marked degree. 1 patient who had recovered considerable voluntary movement died of pneumonia while recovery was still in progress.

Although return of the tendon reflexes was the first evidence of recovery of motor function, simple hyperactivity of the tendon reflexes with the exception of the finger-jerks could not be related to recovery of willed movement. For, with the exception of the finger-jerks, the tendon reflexes in all our patients were hyperactive within forty-eight hours following the onset of hemiplegia. To some extent, a correlation could be made between the return of the finger-jerks and the degree of recovery, but it was certainly not absolute. Of 5 patients who recovered completely, 3 showed hyperactive finger-jerks within forty-eight hours after the onset of hemiplegia, and the other 2 showed hyperactivity of the finger-jerks six and nine days after the onset of hemiplegia. In 5 patients who recovered

no voluntary movement whatsoever, the finger-jerks became hyperactive within forty-eight hours after the onset of hemiplegia in one; while in the others hyperactivity appeared in three, six, seven, and twenty-eight days after the onset of hemiplegia. Patients who ultimately recovered only the flexor synergy required forty-eight hours, and three, nine, and twenty days to develop hyperactive finger-jerks. Of 3 patients showing further recovery, 2 showed hyperactivity of the finger-jerks within forty-eight hours after the onset of hemiplegia while the other showed no hyperactivity until eighteen days after the onset of hemiplegia. Therefore, early return of finger-jerks more frequently presaged a more complete recovery of motor function than late return of finger-jerks. These findings are summarized in Table I.

The time of onset of spasticity paralleled the onset of hyperactivity of the finger-jerks. Although the intensity of spasticity was mild in all the cases at its onset, spasticity never became very intense in patients who later recovered completely. The maximum intensity in these patients was reached within twenty days at the most, after the onset of hemiplegia. In patients who recovered completely, spasticity was not detected in the shoulder. Clonus could be demonstrated in only 1 of these patients, and the clasp-knife phenomenon in only 2. In patients who did not recover completely, spasticity became much more intense in its later development. In 2 of these patients the maximum intensity was not reached until six months after the onset of hemiplegia. 12 patients exhibited spasticity in the shoulder groups as well as in the flexors of the elbow, wrist and fingers. Spasticity in the elbow extensors was encountered more frequently in this group. Wrist or finger clonus was seen in 5 patients and the clasp-knife phenomenon in 2.

The relationship of proprioceptive facilitation and the traction response to the return of voluntary movement was striking. In Table I it will be seen that in the patients who recovered completely, proprioceptive facilitation could be elicited within nine days following the onset of hemiplegia and the traction response within thirteen days. In the patients who did not recover completely these reactions were not elicited until at least fifteen days after the onset of hemiplegia. It will also be noticed that in the latter group, these two reactions could be elicited earlier after the onset of hemiplegia in those patients recovering some independent movement at each joint, than in those recovering only the ability to perform the flexor synergy. These reactions could not be obtained at any time in the patients who did not recover movement of the hand. However, this does not mean that proprioceptive facilitation or the traction response could not be obtained in the absence of voluntary movement or that the ability to elicit these responses was an absolute sign of later recovery of willed movement. One

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striking example was that of a patient who had had a stroke six months prior to admission to the hospital and was left with a spastic hemiplegia with total inability to move the left arm. Nevertheless, in this patient proprioceptive facilitation with finger-jerks could produce a flexor synergy of the arm. Apparently the recovery process had halted at this early stage. In this series it is evident that the 6 patients shown in Table I who did not recover the ability to perform willed movement had not even reached the stage in the recovery process at which proprioceptive facilitation appeared.

We may conclude that the most reliable prognostic sign for recovery from hemiplegia was the time of occurrence of proprioceptive facilitation and the proximal traction response. Although late return of tendon reflexes and late onset of spasticity certainly are poor prognostic signs of voluntary movement, there are exceptions to this rule. Only the occurrence of proprioceptive facilitation and the traction response proved to be infallible prognostic signs of recovery of willed movement.

With the appearance of facilitation by contactual stimuli the previously weak and incomplete movements became greater in amplitude and considerably increased in power of voluntary movement. Ability to perform only one part of the flexor synergy without the others did not begin to take place until willed movements could be facilitated by contact stimuli, but the first signs of contact facilitation could appear in the stage of the flexor synergy.

The grasp reflex could be obtained only in those patients who later recovered completely. It was never obtained in the absence of some voluntary movement. Movement was gravely defective in the presence of spasticity. With the return of the grasp reflex, spasticity of the wrist and finger flexors abruptly diminished. At this time, both power and range of movement increased and dexterity greatly improved. Prior to the appearance of the grasp reflex, flexion and extension of the fingers was slow and clumsy. Opposition of the thumb to all the fingers was extremely difficult; at this time in no case could the thumb be opposed to the tips of the fingers, nor could the thumb be opposed to the little finger. Attempts to move one finger alone usually resulted in an associated flexion of all the fingers. In several cases the index finger could be feebly moved alone prior to the appearance of a distinct grasp reflex, but attempts at movement of the little finger caused an associated flexion of the ring finger. Following the appearance of the grasp reflex, opposition of the thumb to all the fingers could be performed with a great degree of rapidity and dexterity. Movements of one finger alone could then be performed without causing associated movements of other fingers, and fatigue was considerably reduced.

If vision was excluded, movement was performed only with great difficulty prior to the appearance of the grasp reflex. Any willed movement was then diminished in speed and dexterity if the patient was not allowed to watch what he was doing. In attempting to oppose the thumb to each individual finger, the patient failed to oppose the thumb and fingers in several instances and missed one or two fingers entirely. This motor defect occurred even though no disorder of sensory perception could be demonstrated. With the appearance of the grasp reflex the motor defects introduced by the exclusion of vision were found to be markedly reduced. Occasionally there was some hesitancy before beginning a movement, but the marked ataxia and inability to execute certain more difficult movements such as finger-thumb opposition did not occur. With complete recovery and final disappearance of spasticity exclusion of vision did not cause any movement defect whatsoever.

Discussion

Our investigation revealed that hemiplegia, except in a late stage of its most severe and complete form, is neither static nor stereotyped. Great variation was found in each of the classical criteria of distribution of paralysis and process of recovery. This is manifestly determined in part by differences in the situation and type of causative lesion. Nevertheless, in this series of cases an orderly progression of associated phenomena was found to characterize the course of events in any particular muscle group. The process of recovery in the paralysed hand or foot was a constantly evolving series of reactions and followed a general pattern with some variations. With the onset of hemiplegia the affected limbs were completely paralysed, with diminution of the tendon reflexes and resistance to passive movement. Within forty-eight hours the tendon reflexes became hyperactive and resistance to passive movement increased in the wrist and finger flexors and the plantar flexors of the ankle. This resistance became more intense over a period of time and involved other muscle groups, particularly the flexors and adductors in the upper limb, and the extensors and adductors in the lower limb. The tendon reflexes became more brisk and sometimes clonic.

The return of voluntary movement appeared first as flexion at the shoulder and hip. Later flexion of the elbow, wrist and fingers, and knee and ankle were added to these movements. At this time any attempt at willed movement resulted in a flexion of the shoulder, elbow, wrist and fingers, or hip, knee and ankle together. Thus the "flexor synergies" of the arm and leg became manifest as total reactions. In later, but overlapping sequence, the extensor synergies of the arm and leg developed.

When the tendon reflexes had become hyperactive, it was possible to

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facilitate willed flexion of the upper extremity by a series of tendon reflexes and by stretching. At this time the proximal traction response also appeared. This was an enhancement of the spasticity in the flexors at all joints when traction was made on the shoulder flexors and to a less degree when wrist, finger or elbow flexors were stretched. This response could also facilitate willed flexion of the arm. Both the first willed flexion and the traction response activated the same muscles and could be facilitated or depressed by action of the tonic neck and body-righting reflexes. The body-righting reflex had the most profound effect, so that with the patient lying on his side with the paralysed limbs uppermost, both the traction response and the effect of willed effort were greatly facilitated. With the patient lying on his side with the paralysed limbs lowermost, the traction response was abolished and willed movement was extremely weak and limited in range. Our attention had been directed to the proximal traction response in a study of hemiplegia in the monkey following ablation of area 4 and section of the medullary pyramid, of which a preliminary note has been published elsewhere (Denny-Brown, Twitchell and Saenz-Arroyo, 1949). In such experiments this response was utilized by the animal in the first recovered spontaneous movement. We were convinced that in the monkey it is identical with the reflex grasping of the thalamic animal, and was primarily a body-righting reflex. The relationship found in this study identifies the same responses as the first stage in recovery from hemiplegia in man, and its development as the first willed movement.

It was therefore clear that in its beginning, the return of ability to flex the fingers was a part of the total flexor synergy of the arm, and occurred together with flexion of the wrist, elbow, and shoulder. The next event in recovery of movement was the occurrence of ability to flex either shoulder, elbow, all the fingers, or wrist, each without the others. This separation of the elements of the synergic complex was only gradually achieved. While it was still only incompletely attained, it was found that flexion of all the fingers together could now be greatly facilitated by contactual stimulation of the palm of the hand. If power and dexterity of voluntary movement continued to improve, a stage was reached where spasticity abruptly lessened, first in the shoulder and elbow muscles, and later in the flexors of the wrist and fingers. In close association with this decline of spasticity in the wrist and finger flexors the grasp reflex returned, and with it the first ability to perform independent movement of the fingers. The effect of a contactual stimulus moving distally in the palm was no longer just facilitation of willed effort, but alone was adequate to initiate the small active flexion which Seyffarth and Denny-Brown (1948) termed the catching phase, and upon which stretch of tendons

elicited the proprioceptive phase of the grasp response. Further, this reaction could be fractionated by the limitation of the stimulus to the palmar surface of one finger, then inducing a "catching" flexion only of that finger. Coincident with the appearance of such fractions of the grasp reflex there was found the ability to move each finger independently. Finally, when willed movement of the affected limb became as rapid as dexterous as the unaffected, spasticity disappeared completely.

The course of recovery has been more particularly studied in relation to the use of the hand and upper limb, though the data accumulated regarding the recovery of the lower limb indicated that a similar series of changes was occurring. Whereas the primary events of recovery in the upper limb are associated with the performance of prehension, and therefore flexor reactions, those of the lower limb soon became dominated by extensor activity. We have not attempted to determine the significance of such extension, though it is clearly related to the reflex mechanisms of walking and standing.

Recovery of movement in the upper limb could in general be divided into three distinct stages, the first being dominated by proprioceptive reactions, the second by contactual stimulation of the extremity, and finally a seeming total independence of movement upon such externally applied agents. It was apparent that vision had a facilitating effect in the first two stages, but at a period when the grasp reflex had become well developed, exclusion of vision gradually ceased to cause any resulting defect in the performance of movement. Movement freely projected in space without visual control is the last accomplishment to be attained.

Our findings indicate that the different phases of the return of ability to make willed movements in hemiplegic limbs are associated with the appearance of a series of responses each of which is derived from stimulation of the limb concerned. In the earliest stages the basic responses are simple proprioceptive and contactual reactions. Their successive modification as recovery proceeds allows the assumption that the ability to move a part by effort of will alone is itself a modification of these elementary contactual and proprioceptive reflexes. The static spasticity of residual states when power of voluntary movement remains minimal or absent is derived from imperfect integration of these segmental responses. Though this study does not attempt to provide the explanation for the relatively greater spasticity of some residual states compared with others, it does indicate that the absence of voluntary movement is associated with a relative absence of motor adaptation as a whole.

These findings provide further evidence for the thesis advanced by Denny-Brown (1950) that the rolandic region of the cerebral cortex is a "strereognostic apparatus for exploring space," based upon elaboration

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of contactual modifications of proprioceptive reactions. He pointed out that the first event in disintegration of motor function in progressive frontal lobe lesions is commonly the release of certain cortical motor automatisms, such as instinctive grasping, from their natural integration with total behaviour. When these motor reactions become impaired, the relatively coarse triggering of proprioceptive reactions by contact stimuli, such as the grasp reflex, makes its appearance. Finally, with the loss of the contact conditioning, the proprioceptive reactions are fully released in the form of spasticity. In recovery of function the reverse sequence could occur. The present investigation of a large number of cases of cerebral hemiplegia reveals the regularity of operation of the same factors in the sequence of recovery of function. The steps in recovery from loss of motor function in the disorder known as hemiplegia begin with simple and then more complex proprioceptive reactions. These in turn become modifiable by contactual reactions, each of which is soon adapted to the purpose of will.

The great disability which results when recovery is halted in the phase of heightened proprioceptive activity has prompted many earlier investigations. Walshe (1919) clarified the previously confused views as to the nature of spasticity, and showed its identity with the type of exaggeration of postural reflexes seen in decerebrate rigidity. The analysis of Sherrington and his collaborators subsequently identified the stretch reflex as the fundamental reaction of such disorder. It has often been assumed that if spasticity could be abolished, willed movement could be more effectively performed. Though this might be possible in certain spinal disorders, the present study indicates that the first movements to appear following hemiplegia are themselves facilitated stretch reflexes. The problem at that stage is not so much to abolish the spastic reaction, as to harness its diffuse hyperactivity.

The return of the tendon reflexes (with the exception of the finger-jerks in several instances) was found uniformly to be the earliest event in the course of motor recovery. This was closely followed by the first evidence of heightened response to sustained stretch. In its first appearance the returning stretch response was a soft, yielding resistance felt at the end of a full range of passive stretch of the flexor and adductor muscles of the arm and the extensor and adductors of the leg. It appeared first in the wrist and finger flexors and ankle plantar flexors, then in the elbow flexors and knee extensors, and still later in the retractors and adductors of the shoulder and extensors and adductors of the hip. At its full development increased resistance to passive stretch showed the generally recognized qualities of spasticity, for the resistance in any muscle group when encountered rose to a maximum as stretch was continued

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and abruptly declined towards the end of passive movement. In the course of development of spasticity in any muscle group the resistance to passive stretch appeared earlier in the course of passive lengthening of the muscle. The clasp-knife phenomenon was of late appearance, in general within two to four weeks after the first appearance of increased resistance, and was observed in the flexors of the elbow and the extensors of the knee. In the presence of clonic tendon reflexes the initial peak was well developed, the subsequent decline rapid, and at times rhythmical subsequent peaks of resistance showed the well-known relationship between the occurrence of clonic tendon reflexes and "sustained clonus." We therefore regard the clasp-knife phenomenon and clonus as having some general relationship. It was not possible to correlate the appearance of the clasp-knife phenomenon or clonus with any variation in the quality or intensity of spasticity. They occurred in patients who made a complete recovery and in patients who never recovered the ability to produce movement by effort of will alone. It was apparent that the resistance to passive movement and the tendon reflexes did not always develop in parallel manner. That is, these reactions did not necessarily become exaggerated or subside at the same time. Thus it was seen that the tendon reflexes could remain hyperactive for a long time before spasticity made its appearance. And in one patient the finger-jerks became clonic after the subsidence of spasticity in the finger and wrist flexors, with increasing power of willed movement.

The appearance of spasticity of some degree in the flexor groups of the upper limb, the extensor groups of the lower limb, and the adductor groups of both limbs was general in the series of cases studied. "Flaccidity" was a transient phenomenon in these muscles, although there was great variation in its duration. Some spasticity appeared in addition in the opposing muscles, particularly in the extensors of the elbow and the flexors of the knee, in about one-fifth of the patients, but was without significance in relation to course or ultimate recovery. On general principles, anomalies in the duration of flaccidity, and in the distribution of paralysis and spasticity may be expected to be related to the extent and location of the cerebral lesion. As no autopsy material is available from the case material presented, we have not attempted such correlation. Although there was not complete correlation, there was a suggestion of poor prognosis for recovery if the period of "flaccidity" was long. We were not able to determine any difference between the spasticity of the completely paralysed hand, and that which preceded return of voluntary power, except that the latter was, in those cases in which it was observed, more easily modified by neck and body-righting reflexes, and by traction on the proximal segments of the limb. Early return of

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the proximal traction response, and of facilitation of willed flexion of finger flexion by a series of finger-jerks had good prognostic significance for later recovery of willed movement.

The course of recovery from cerebral paralysis does not favour the division of motor function into separate independent entities such as segmental reflexes, neck reflexes, labyrinthine and body-righting reflexes and optic-righting reflexes. Each of the more complex members of these is composed of elements of the less complex. The ability for willed movement is therefore not a separate and indivisible function. The present study indicates the part played by these factors in the course of recovery from hemiplegia, and provides a rationale for proprioceptive and contactual exercises in the re-training of movement.

Conclusions

If motor function recovers following the hemiplegia caused by a lesion of the cerebrum, the common course of recovery shows a regular sequence of reflex changes, each of which is associated with a corresponding increase in ability for willed movement. The process of recovery may become arrested at any stage in this sequence. After the initial phase of depression of all motor function, the proprioceptive responses become abnormally active. These proprioceptive responses do not constitute a simple entity, for they are modified and conditioned by other factors, such as stretch on associated muscles, the position of the patient's head in relation to his body, and the position of the body in relation to the supporting surface, and later by certain contactual stimulation. As the recovery process proceeds, the more elementary proprioceptive responses become subordinated to special exteroceptive stimulation. Voluntary movement appears as a further facilitation of the available responses at each stage. It is not a separate entity, but from its first appearance it takes the form of conditioned proprioceptive and contactual responses.

I wish to express my gratitude to Professor Denny-Brown for his advice, assistance and criticism during the course of this investigation.

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THE SEGMENTAL INNERVATION OF THE MUSCLES OF THE HAND

BY

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MUCH remains to be known with certainty about the segmental innervation of the muscles of the limbs and any investigations that can throw light on this matter are worth recording. That there is an underlying plan of segmental innervation is certain, and the writer has recorded elsewhere (1949) his conclusion that the principles of motor innervation of the limbs indicate the existence of spinal centres for joint movements. These centres in the anterior grey columns appear to be for the lower motor neurones what the cortical centres of area 4 are for the upper motor neurones. They do not control individual muscles as such, but each centre controls the complex of a joint movement. In most cases a joint movement is controlled by a centre that occupies two adjacent spinal segments and the opposite movement is controlled by a centre in the next two segments. Thus, the complete centre for a joint typically occupies four continuous segments of the cord. Further, joints placed more distally in the limb are controlled by centres lying lower in the cord: for a joint one segment more distal in the limb the joint innervation centre lies, *en bloc*, one segment lower in the cord. Thus the lowest segment in each enlargement (Th 1 and S 3) is distributed to the intrinsic muscles of hand and foot respectively.

In the case of the upper limb certain joint movements are controlled not by two segments but by only one, and this is very likely due to a breaking up of the relatively simple centres of the quadrupedal forelimb into more discrete centres for better control of the more precise movements of the human forelimb. The intrinsic muscles of the hand, for example, are supplied from only one segment, namely Th 1.

The spinal centres differ from those of the cortex in being inaccessible to experimental stimulation. They are long and they overlap each other, and it is impossible in animal experiment to limit a stimulus to one centre alone, as the writer has found. Thus less direct evidence has to be used for establishing the segmental levels responsible for movement in any joint. A mass of clinical evidence exists in man, but for the most part it lacks precise accuracy, since it is usually impossible to assess exactly the extent of a segmental lesion. In the simplest disease or injury,

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of even a single nerve-root, it is often impossible clinically to be certain either that the lesion is complete in that nerve-root or that the adjoining nerve-root does not share at least in part in the lesion.

Much experimental work has been done on this subject. Ferrier and Yeo (1881), Herringham (1886), Sherrington (1892), Bruce (1901), Wilfred Harris (1904), Romanes (1941) and Elliott (1942) have made contributions of value in constructing the picture of spinal centres for joint movements. For example, in 1892 Sherrington showed the spinal cord of an adult cat at a meeting of the Physiological Society. At C 8 the posterolateral group of anterior horn cells was much reduced on one side—the side from which the forefoot had been amputated when the animal was less than a month old. The opportunity of investigating a similar case in man occurred to the writer this year (1950).

Material and Methods

The subject was an adult male who died at the age of 60. The left hand had been amputated at the radiocarpal joint at the age of 16. The whole body was injected in the dissecting room, on the first day with glycerine, spirit and phenol, on the second day with 10 per cent formalin. The brachial plexus was confirmed by dissection to be formed by the normal C 5, 6, 7, 8 and Th 1 in the ordinary way. The cervical and upper thoracic cord was removed and divided into its segments by transection half-way between the attachments of the nerve rootlets. The lengths of the segments were:

C 6	12 mm.	Th 1	11 mm.
C 7	12 mm.	Th 2	11 mm.
C 8	10 mm.		

Each segment was imbedded in paraffin, cut at 20μ and mounted serially. The sections were stained with hæmatoxylin and eosin and the business of counting the cells began.

Findings

It became apparent from the first that the grouping of the large multipolar cells of the anterior grey columns was not constant. In some sections they fell into groups easily recognizable as those described by Sherrington, Bruce and Romanes (figs. 1 and 2), in other sections the cells of the anterior horn were scattered like currants in a bun and had no distinguishable grouping. Further, there was a regular fluctuation between the two types of cell distribution, and it became apparent that the spinal motor nuclei do not occur as regular cylindrical masses in the grey columns but rather as a series of beads lying vertically. Where the cells occurred in groups they were counted in such groups; where they were scattered they were counted in the areas occupied by the known

groups. An error in counting one such group is compensated by an error of the opposite sign in the adjoining group. Another point to be noted is the large size of the multipolar cells of the motor nuclei. Cells cut across appear in more than one section and must be counted more than once. Counting the cells in alternate sections and doubling the totals

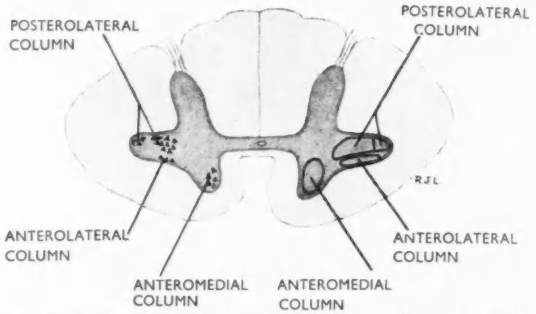

FIG. 1.—The grouping of the motor cells in the anterior horn.

probably gives a more accurate cell count than adding the totals for every section. Both methods were used. It is not particularly relevant to this investigation, however, since it is the comparison between the two sides rather than the total number of cells present that is under consideration, and the error of counting one cell twice would occur equally on the two sides.

THE FIRST THORACIC SEGMENT

This segment measured 11·0 mm. in length, and thus 550 sections were counted. The grouping of the large multipolar cells of the anterior horn falls naturally into the areas described by Sherrington, Bruce *et al.*, and is indicated in figs. 1 and 2.

The anteromedial columns.—The anteromedial columns occur along the whole spinal cord and are not confined to the limb enlargements; their cells control the flexor and extensor musculature of the trunk and spine, and have nothing to do with the limbs. The cell counts of these columns were symmetrical, as was to be expected. The totals were 1,540 on the left and 1,680 on the right. It is of passing interest to note that on each side they are over twice as plentiful in the lower half as in the upper half of the segment (Table I, p. 489). This suggests that only the lower half of the segment is concerned in the innervation of the first intercostal muscle. There are no subgroups of the cells in the anteromedial columns, but the beading is indicated by a regular fluctuation in the number of cells seen in serial sections.

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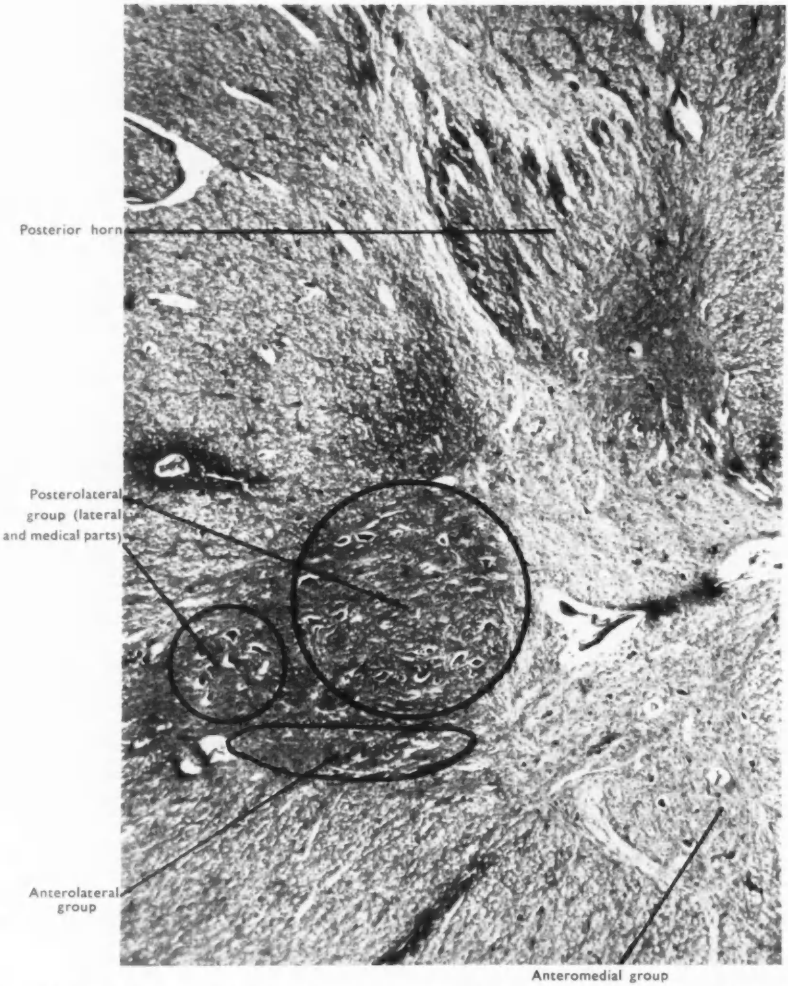

FIG. 2.—A photograph showing typical grouping of the motor cells of the anterior horn. Upper part of Th 1 segment.

The cervical enlargement.—The cervical enlargement, or mass of grey matter lying lateral to the anteromedial grey column, is known to contain the cells of the motor nerves to the limbs. It occupies only the upper 6·5 mm. of Th 1 segment, the lower 5·5 mm. of which contains a slender anterior horn like that of the whole thoracic part of the cord.

The anterolateral group (fig. 3, Table II): This group is small and dies out 1·5 mm. above the lower end of the cervical enlargement. The cell counts are symmetrical in the upper 2 mm. of the segment (right

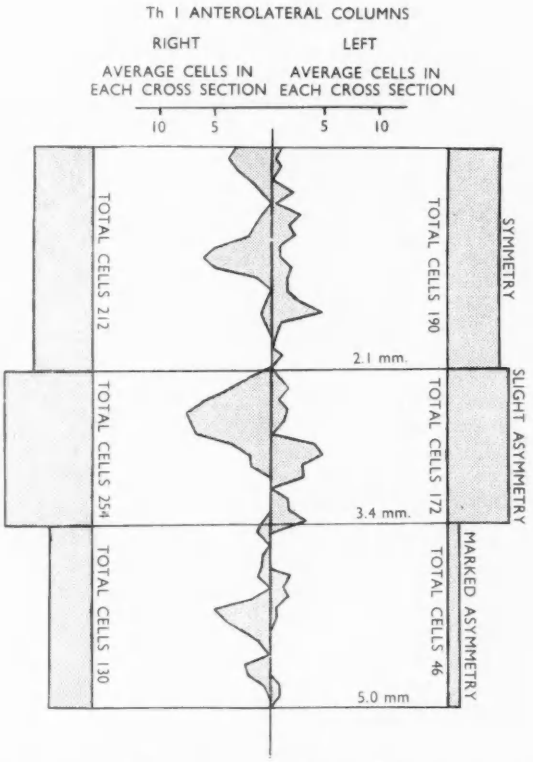

FIG. 3.—The cell counts of the anterolateral columns of Th 1 represented graphically. The columns occupy only the upper 5·0 mm. of the segment.

212, left 190 cells). In the next millimetre a diminution begins on the left side, and in the last 2 mm. there is a 3 to 1 asymmetry.

The posterolateral group (fig. 4, Table III): In this group are included all cells lying behind the anterolateral group. Its position is shown in figs. 1 and 2. The total cell counts of this group are stated in Table III and represented in graph form in fig. 4. There is symmetry in the upper 2 mm. of the segment, asymmetry commences in the next millimetre and is marked in the lowest 3 mm., right to the bottom of the cervical enlargement, where the right side outnumbers the left by 3 to 1. The posterolateral group contains, however, two subgroups of cells, a larger medial and a smaller lateral group. These are very distinct from each other in such sections as that shown in fig. 2, but due to the beading already mentioned they overlap each other very considerably in other sections. An attempt has been made to count the medial and lateral

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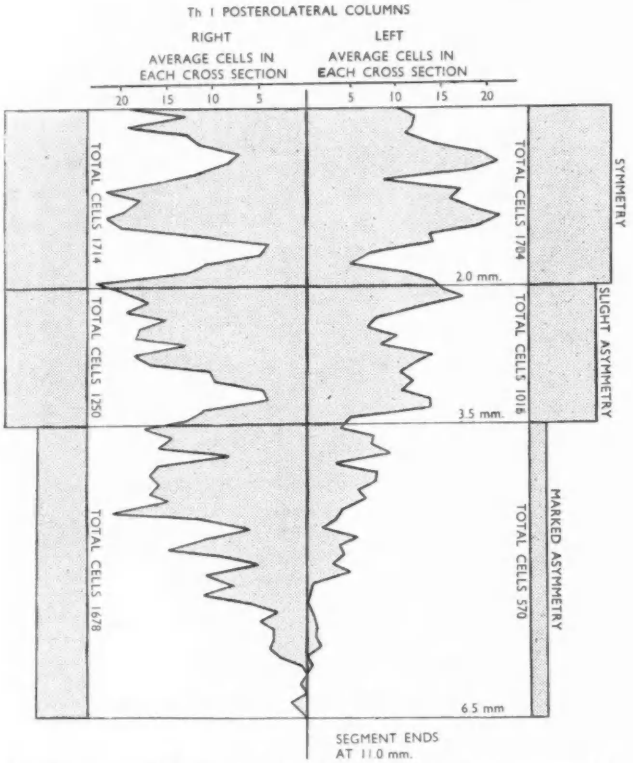

FIG. 4.—The cell counts of the posterolateral group of Th 1 segment. The group ends at 6·5 mm., though the segment is 11·0 mm. long.

groups separately and the result is indicated in Tables IV and V and figs. 5 and 6.

The larger medial group of cells in the posterolateral columns shows symmetrical counts down to 2 mm. In the next 1·5 mm. there is a commencing asymmetry which becomes marked (3 to 1) in the next 3 mm., down to the distal extremity of the cervical enlargement.

The smaller lateral group of cells shows a slightly different level of asymmetry. The marked asymmetry does not commence until about 4 mm. and the group dies out at 6 mm. The asymmetry is only about 2½ to 1 here, as against 3 to 1 in the other groups.

The Eighth Cervical Segment

There is no asymmetry in any of the groups in the anterior grey columns of this segment. The cell counts are recorded in Table VI.

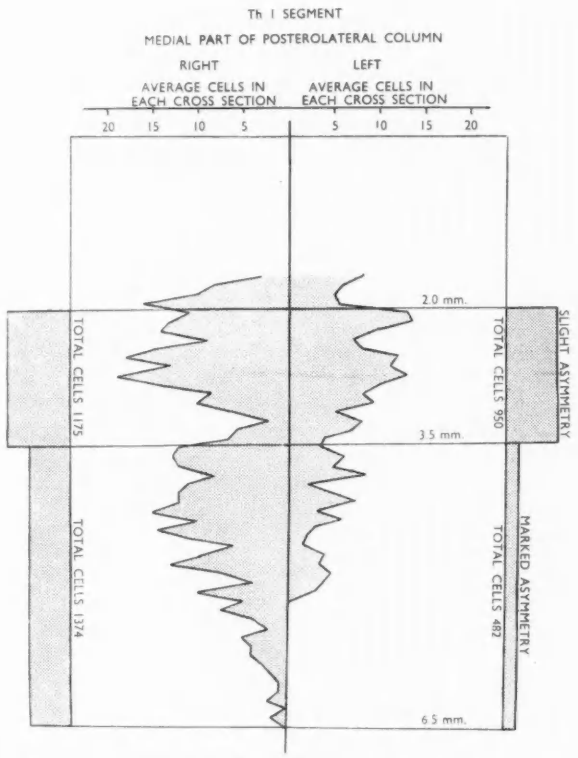

FIG. 5.—The asymmetry in the medial part of the posterolateral columns.

DISCUSSION

In the case of C 8 and the upper 2 mm. of Th 1 segment, such asymmetry as occurs is slight (about 10 per cent) and is not outside the limits of experimental error in counting the cells. Marked asymmetry occurs in only the lower part (4·5 mm.) of the cervical enlargement and is here of the order of 3 to 1. It commences at slightly different levels for the three cell groups of the cervical enlargement and these cell groups are found to terminate at different levels. The large multipolar cells of the anterior horn, so reminiscent of the Betz cells of cortical area 4, have disappeared in a situation that must be assumed to be the centre for the missing intrinsic muscles of the hand. Certain other muscles that remain in the forearm are virtually functionless, for example, the long flexors and extensors of the digits, whose tendons were fixed in scar tissue at the distal end of the radius. Section of these muscles, however, shows no degeneration, and their motor nerves appear histologically normal.

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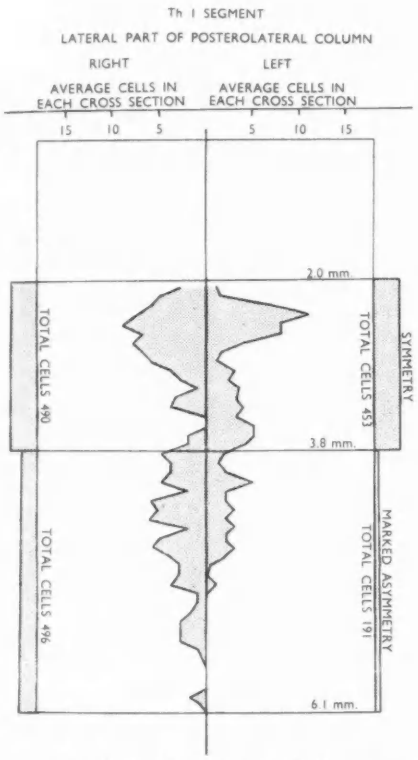

FIG. 6.—The asymmetry of the lateral parts of the posterolateral columns.

Although the muscles have been functionless for over forty years there is no evidence to suggest that their anterior horn cells are not intact.

Assuming the asymmetry to represent the missing cells of the intrinsic hand muscles, the reconstruction of the spinal nucleus shows (fig. 7) a mass filling the caudal extremity of the cervical enlargement and extending upwards therefrom as sausage-shaped prolongations, to a distance of 2 mm. below the upper limit of Th 1 segment. The spinal centre for the hand muscles does not extend into the eighth cervical segment.

The method of comparing cell counts on the two sides offers a means of deducing the situation of spinal centres for joint movements that has been somewhat neglected. It is desirable to have specimens from subjects who have suffered early amputation. If a large series of such spinal cords were examined, in each case checking the limb plexus concerned for the possible presence of prefixation or postfixation, it should be easy to construct maps of the anterior grey columns similar to those of the motor cortex.

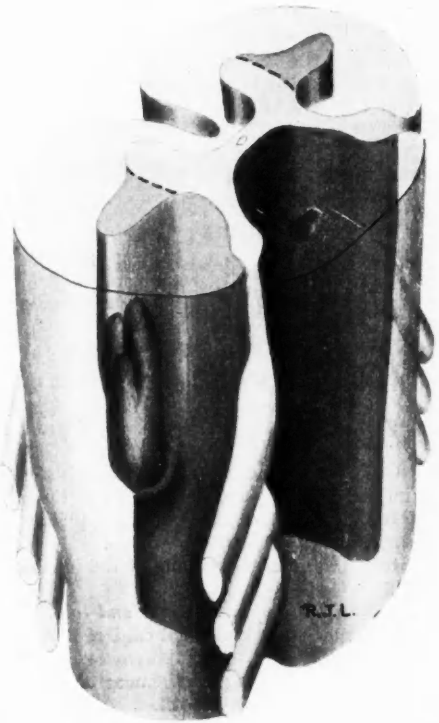

FIG. 7.—Reconstruction of the first thoracic segment. The cervical enlargement occupies little more than the upper half of the segment. The spinal centre for the intrinsic muscles of the hand lies in its caudal end, i.e. in the middle third of Th 1 segment.

SUMMARY

(1) The spinal centre for the intrinsic muscles of the hand appears to be situated in the lowest 4 to 5 mm. of the cervical enlargement (the middle third of Th 1 segment) and does not extend into C 8.

(2) Every opportunity should be taken of doing cell counts of the spinal cord in cases of long-standing amputation.

TABLE I.—ANTEROMEDIAL COLUMNS OF TH 1

	Right	*Left*
Upper 5·5 mm. ...	450	448
Lower 5·5 mm. ...	1,231	1,094
Total in segment	1,681	1,542

TABLE II.—ANTEROLATERAL COLUMNS OF TH 1

	Right	*Left*
Upper 2·1 mm. ...	212	190
Next 1·3 mm. ...	254	172
Lowest 1·6 mm. ...	130	46

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TABLE III.—POSTEROLATERAL COLUMNS OF TH 1

	Right	*Left*
Upper 2·0 mm. ...	1,714	1,704
Next 1·5 mm. ...	1,250	1,016
Lowest 3·0 mm. ...	1,678	570

TABLE IV.—MEDIAL GROUP OF POSTEROLATERAL COLUMNS OF TH 1

	Right	*Left*
Upper 2·0 mm. ...	Symmetrical	
Next 1·5 mm. ...	1,175	950
Lowest 3·0 mm. ...	1,374	482

TABLE V.—LATERAL GROUP OF POSTEROLATERAL COLUMNS OF TH 1

	Right	*Left*
Upper 2·0 mm. ...	Symmetrical	
Next 1·8 mm. ...	490	453
Lowest 2·3 mm. ...	496	191

TABLE VI.—TOTAL CELL COUNTS IN C8 SEGMENT

	Right	*Left*
Anteromedial group	982	899
Anterolateral group	1,164	1,235
Posterolateral group	4,393	4,801

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A CLASSIFICATION OF PERIPHERAL NERVE INJURIES PRODUCING LOSS OF FUNCTION

BY

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SEDDON (1943) has recently directed attention to the unsatisfactory nature of current classifications of nerve lesions. As a result of his wide experience of traumatic nerve injury he advocated a more precise and useful classification which recognized three types of nerve injury leading to loss of function and introduced three new terms to peripheral nerve literature—neurotmesis, axonotmesis and neurapraxia. Details are provided in Seddon's publications but the essential features of these three types of injury were as follows:

(1) "Neurotmesis is the name given to a lesion of such severity that all essential parts of the nerve are destroyed. The simplest and commonest variety of the condition is that resulting from anatomical division, but interruption of the same kind can occur without any apparent loss of anatomical continuity. Wallerian degeneration occurs peripherally and the clinical picture is that of complete interruption of the nerve. Spontaneous recovery is rare, and never of good quality."

(2) "Axonotmesis is a lesion characterized by complete interruption of axons, but with preservation of the supporting structures of the nerve —Schwann tubes, endoneurium and perineurium. . . . The local lesion, when seen some time after infliction of the injury, may be almost indistinguishable from normal nerve, though occasionally there may be a 'fusiform neuroma.' Histologically, there is complete interruption of the axons, preservation of the Schwann tubes and endoneurium, and Wallerian degeneration peripherally. Clinically, the condition is indistinguishable from neurotmesis until recovery occurs, which, in axonotmesis, is spontaneous."

(3) "Neurapraxia is a lesion in which there is no axonal degeneration, though there may, perhaps, be a localized degeneration of the myelin sheaths. . . . Recovery is spontaneous and complete, and so rapid that it cannot be explained in terms of regeneration following Wallerian degeneration . . . and there is no anatomical 'march' of recovery such as is seen after nerve suture or axonotmesis."

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Though this classification greatly clarified the position certain objections have been raised to its acceptance. These were directed primarily at a classification which introduced rather complicated terms requiring, for their understanding, some knowledge of Greek. A consideration of the prerequisites for medical education indicates, however, that the practitioners of the future are unlikely to possess this knowledge without which the terms become as obscure as those they were designed to replace and at best would involve the memorization of the condition to which each referred.

There are, however, other limitations which restrict the usefulness of the classification. According to Seddon "axonotmesis is a lesion characterized by complete interruption of axons, but with preservation of the supporting structures of the nerve—Schwann tubes, endoneurium and perineurium." Such an injury should be followed by complete restoration of function and the absence of neuromata. However, Seddon states elsewhere that "occasionally there may be a fusiform neuroma" and implied in two statements that recovery in axonotmesis may be incomplete: "The quality of recovery is excellent, usually perfect" and "after axonotmesis muscles regain their power and volume fairly rapidly . . . and sometimes completely." These two observations suggest that in some cases regarded by Seddon as examples of axonotmesis the injury may have been more extensive than his definition indicated. That he was aware of this is apparent from the following statement: "At one extreme the term is strictly applicable: if the nerve is very nearly normal in appearance and consistency, it may fairly safely be assumed that the lesion is confined chiefly to the axons, which will exhibit spontaneous regeneration along their old paths, leading to perfect restoration of function. After this, there is every grade of intraneural damage, leading finally to those lesions in which the destruction of the endoneurium and its replacement by irregular fibrous tissue is so great as to prevent any spontaneous regeneration." Unfortunately no allowance was made for this in the classification which fails to distinguish between the lesion in which the axon coverings are intact and that in which the damage is more extensive.

It is, however, important to distinguish the injury, excluded by the definition of axonotmesis and not included in his classification, in which the axons and their immediate sheaths are interrupted while the perineurium, and therefore the funiculus, remains in continuity. Such injuries, as we shall see, are associated with variable effects at the periphery and may be followed by incomplete recovery because regenerating axons may now escape from the endoneurial tubes which they originally occupied. The confusion of axonal growth which is produced in this way results in some axons entering foreign tubes which means that these fail to re-

establish continuity with the appropriate end-organ. This is also the type of lesion which occasionally gives rise to a fusiform neuroma.

In an attempt to overcome these objections a new classification is proposed which is based essentially on a detailed investigation of the anatomy of peripheral nerves and a long-term study of over 300 cases of peripheral nerve injury. It has the merit of simplicity in that it is based on the normal anatomy of the nerve trunk and makes no great demands on our knowledge of nerve conduction while it is sufficiently embracing to cover all types of traumatic injury producing loss of function. Furthermore the terminology employed is clear once the fundamental structure of the nerve trunk is appreciated. Before proceeding to a consideration of the types of nerve injury that may result from trauma to a nerve it will be necessary, therefore, to refer briefly to the structure of the nerve trunk. Though elementary, this is nevertheless fundamental to an understanding of nerve injury and no apology is made for including it.

Four components of the nerve trunk are relevant to the discussion: the axon, the axonal sheath, the funiculus and epineurium.

(1) *The axon.*—This comprises the conducting element of the nerve trunk.

(2) *The axonal sheath.*—This is composed of three layers of tissue which are arranged concentrically about the axon. A single layer of Schwann cells is applied to the surface of the axon. Outside this are two connective tissue membranes, an inner fine neurilemma and an outer slightly denser endoneurium. In some nerve fibres an additional substance of variable thickness, myelin, is interposed between the Schwann layer and the axon. This substance is not arranged continuously along the whole length of the axon but is interrupted at intervals where the Schwann cell cytoplasm establishes contact with the axon—these intervals are the nodes of Ranvier.

The axon and its sheath collectively comprise the nerve fibre. The outer limiting membrane of the fibre is the endoneurium and may be regarded, for our purpose, as forming a tube which contains the other elements.

Following severance of the axon the contents of the endoneurial tubes below the injury fluctuate, in both quantity and composition, throughout the various phases of degeneration but ultimately they are entirely the products of Schwann cell proliferation. If the outlines of the endoneurial tube are preserved the regenerating axon is confined throughout regeneration to its original tube so that the reconstitution of the fibre pattern is inevitable. If, on the other hand, the wall of the tube is ruptured or the tube is blocked by fibrosis developing as the result of either

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the original injury or ischæmia secondarily induced, the regenerating axon may escape into the surrounding tissues or may fail to pass the fibrotic obstacle which has become interposed in its path. In either case the axon fails to re-establish a connexion with the end-organ originally innervated by it and as a consequence the quality of the recovery is adversely affected.

(3) *The funiculus.*—Each funiculus is composed of a number of nerve fibres invested in a sheath of connective tissue, the perineurium. The funiculi vary in size, their diameter ranging, in nerves preserved in formalin, from 0·04 mm. to 3 mm. Some bundles are traversed by fine septa which are continuous at the periphery with the perineurium. A knowledge of the fibre composition of the bundles comprising the nerve trunk provides the key to an understanding of many of the obscure phenomena associated with nerve injury.

It is uncommon for human peripheral nerves to be composed of a single funiculus. They are, on the contrary, usually composed of several funiculi which, by their repeated division and anastomosis, engage in plexus formations along the full length of the nerve. As a result of these changes both the number and size of the funiculi vary from level to level while the funicular pattern alters so rapidly that transverse sections taken more than a few millimetres apart fail to present precisely the same pattern. The plexus formations also effect a regrouping and funicular redistribution of the component nerve fibres as they are traced proximally from the point where they leave the nerve trunk as individual branches (Sunderland, 1945; Sunderland and Ray, 1948).

The dispersal and funicular redistribution of the fibres occasioned by the funicular intercommunications is effected as follows. The fibres representing individual branches at first pursue an independent course either as a single funiculus or as a compact bundle group in which the funiculi engage in plexus formations. Over this part of their course the fibres are consequently sharply localized though they do not necessarily maintain the same quadrantic relationship as they ascend since migration sometimes carries them obliquely through or over the surface of the nerve.

The bundles of adjacent but independent bundle groups subsequently anastomose, thereby effecting a blending of the constituent fibres of originally distinct groups. An extension of this process ultimately results in the widespread diffusion and blending of fibres from several sources. The scattering of fibres produced in this way occurs gradually, however, and at any one level only a minor degree of intraneural shift is effected. It is the summation of changes at successive levels as the intercommunications are repeated which is ultimately responsible for the widespread intermingling and dispersal of fibres. The latter is achieved, therefore,

only after the fibres have ascended considerable distances along the nerve. Thus the localization of any particular branch system is at first discrete, then discrete in combination with other fibres, and finally a predominant one only, until fibre-diffusion reaches a stage where it cannot be claimed that there is any localization: at this stage the constituent fibres of the bundles are arranged in varying combinations and proportions though each bundle does not necessarily contain fibres from all branches.

For these reasons the longer the course of the fibres of a branch within a nerve trunk, the greater the diffusion and the intermingling of its fibres at proximal levels. When, however, the bundles of a branch with a very high origin commence to anastomose they do so with bundles which have acquired fibres from most, if not all, of the distal branches. As a result the fibres of such proximal branches are rapidly mixed with those from several sources but, since their intraneural course is too short to permit extensive scattering, they remain relatively discretely localized.

Nerve funiculi are, therefore, of two types and both occur together at the same level. There are those which are composed solely of fibres from one branch while the others contain fibres from several sources in varying combinations and proportions. The consequences of a funicular injury in which the endoneurial tubes are ruptured are not the same in each case. A full consideration of the implications of this statement, however, will be deferred until third degree nerve injury is discussed.

(4) *The epineurium.*—The bundles are loosely held together by areolar connective tissue which comprises the epineurium. This tissue is somewhat condensed at the surface of the nerve so that the bundles are held more securely together as a group and the nerve trunk is clearly demarcated from the surrounding tissues in which it is free to move.

Five Degrees of Nerve Injury

Five degrees of nerve injury may now be defined on the basis of changes induced in the normal structure of the nerve. The injuries are arranged in ascending order of severity from the first to the fifth degree and affect successively (i) conduction in the axon, (ii) the continuity of the axon, (iii) the endoneurial tube and its contents, (iv) the funiculus and its contents, and finally (v) the entire nerve trunk. Thus the classification is based on the effect of the injury and not on the cause. It is not the purpose of this communication to elaborate on the latter but it should be noted that these injuries can be caused by a great variety of agents—mechanical, thermal, chemical and ischæmic. The same agent may produce any one of the first four degrees depending on its intensity and the time for which it operates while mechanical deformation can be responsible for all five. Finally, the histological changes initiated by division of a nerve and associated

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with the regeneration which ultimately follows have been treated so exhaustively elsewhere that these features will not receive further treatment in this paper.

First Degree Injury

A first degree injury is sustained when conduction along the axon is interrupted at the site of the injury, there being no break in continuity of the structures comprising the nerve trunk; if the latter shows changes these are of a minor nature. Axonal continuity between the neuron and end-organ is preserved, there is no Wallerian degeneration and the disturbance which is responsible for blocking conduction is fully reversible. After a dormant period the nerve fibres suddenly reawaken to activity, the affected parts commence to function and ultimately recover completely. This type of injury was originally described by Erb (1876) as the "intermediate form" of partial lesion and more recently defined by Seddon (1943) as neurapraxia.

Pathology.—This is the injury about which we know least and consequently find it necessary to write most. Since the condition is inevitably followed by rapid and complete recovery human material will rarely become available for histological examination. In a case of sleep palsy of the radial nerve which came to autopsy twenty-five days after the onset of paralysis Dejerine and Bernheim (1899) made the significant observation that Wallerian degeneration was present only in the branch to brachioradialis. An additional observation was made by Briscoe (1925) who reported that pressure on the phrenic nerve may cause complete paralysis of the relevant half of the diaphragm without producing histological changes in the nerve which can be demonstrated in post-mortem material by the Marchi and Weigert-Pal methods.

Further information has been provided by investigations in which this type of injury has been induced experimentally. Weiss and Davis (1943) effected a pressure block by applying arterial sleeves to the peroneal and tibial nerves in the rat which constricted the nerves. They claim that "a fiber of morphologically sound appearance may yet be inoperative physiologically" so that "histological continuity of nerve fibers does not necessarily imply passage of impulses." When signs of degeneration were present they attributed them not to ischæmia of the compressed segment but to the arrest of "the centrifugal flow inside the axon of substances or factors vital for the maintenance of axonal integrity."

Denny-Brown and Brenner (1944*a*, *b*) blocked conduction temporarily by compressing nerves by direct pressure, tourniquet and spring clip, and studied the histological picture at the site of compression. Signs of damage appeared early and involved swelling, notching and vacuolation of the axons and a change in the staining qualities of the axoplasm. The

compressed section of the nerve became œdematous and was infiltrated with lymphocytes and macrophages. The myelin showed granulation, fissuration and vacuolation, particularly in the vicinity of the nodes and of the Schwann cells; these changes finally resulted in parts of the axon becoming bared or being left with only a thin coat of myelin. There was no, or very little, Schwann cell activity. In some specimens beading of the axons and myelin was observed below the site of compression. Conduction was blocked for periods up to nineteen days, and was then followed by rapid and complete recovery. The histological changes outlasted the return of conductivity, however, and Denny-Brown and Brenner were uncertain whether they were ever fully corrected.

In view of evidence that (i) conductivity is restored before the histological changes associated with nerve block are corrected, (ii) nerve block may exist without any detectable modification of nerve morphology and (iii) nerve fibres with grossly modified sheath structure may continue to function efficiently (Sunderland, 1951), it may be concluded that, in first degree injury, the fundamental disturbance leading to interruption of conduction following compression is one which involves the axon and not its sheaths though we are unaware of the changes which are responsible.

On the basis of their findings Denny-Brown and Brenner (1944*a*) concluded that the transient nerve block associated with "compression of mammalian nerve without angulation must be effective through the related ischemia"—a conclusion which is in general agreement with the observations of others (Lewis, Pickering and Rothschild, 1931; Clark, Hughes and Gasser, 1935; Grundfest, 1936; Thompson and Kimball, 1936; Weddell and Sinclair, 1947; Merrington and Nathan, 1949). An ischæmic mechanism seems to have been clearly established in those cases in which the nerve had been compressed for several minutes. It remains, however, to explain how ischæmia could produce the prolonged block which occasionally follows the application of a force which acts only momentarily. In these cases the ischæmia must be of a very temporary nature though it is possible that changes induced by it may persist and that greater lengths of the axon may also be involved. However, this hardly explains why transient forces may lead to a paralysis which outlasts that induced when the nerve is rendered ischæmic for a much longer period. This rather suggests that in some cases at least the mechanical violence is directly transmitted to, and deforms, the axoplasm and in this way interrupts conduction. Characteristic differences between nerve block due to pressure itself and that due to ischæmia have been demonstrated in acute experiments by Gasser (1935) and by Bentley and Schlapp (1943*b*). According to Gasser "blockade by compression is only slightly reversible, while fibers blocked under a sphygmomanometer cuff

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are restored within two minutes after being released from pressure." Bentley and Schlapp found that the development of nerve block due to pressure is much slower and that persistence of the block for some hours after the release of pressure is in marked contrast to the rapid recovery which followed relief of ischæmia.

Embarrassment of a "centrifugal flow inside the axon of substances or factors vital for the maintenance of axonal integrity" as a contributing factor to the block also requires consideration. The nucleus and perinuclear territory of the neuron are known to contain important energy-producing mechanisms which involve, *inter alia*, the breakdown and synthesis of nucleoproteins. It is conceivable that materials which are essential for the survival and efficient functioning of the processes are made available from the cell body by such a centrifugal flow as Weiss and Davis (1943) have suggested.

Excluding drugs, ischæmia and cold, all of which influence conduction by modifying metabolic processes, injuries producing the type of lesion under review are alike in that they deform the fibre and in doing so reduce its internal dimensions (e.g. stretch and compression). It may be that the proximo-distal flow of essential materials is impeded by this deformation so that the molecular structure of the axoplasm is altered sufficiently to interrupt conduction but not to threaten the survival of the axon. When the survival demands are no longer satisfied axonal disintegration and Wallerian degeneration occur. This concept of disturbed axoplasmal flow has certain attractive features. It emphasizes the importance of the axon and this is consistent with other evidence which excludes the remaining components of the nerve fibre. It would also explain variations in the severity of the nerve injury as evaluated by the duration of the latent period between injury and the onset of recovery. The time taken for the recovery of conductivity subsequent to the restoration of an adequate axonal flow would presumably depend on the degree of deterioration which required correction by the replacement of essential materials and the rate at which these were provided. Latent periods of short duration would indicate minimal obstruction to axoplasmal flow and a rapid restoration of the axoplasm to a functional level. On the other hand latent periods of long duration would represent the additional time required to correct a more serious depletion of axoplasmal materials after the obstruction had been removed. If, however, the mechanism responsible for interrupting the proximo-distal flow is unrelieved the axoplasm below the block continues to deteriorate until finally disintegration and Wallerian degeneration follow and the condition passes from a first to a second degree injury.

Some phenomena, however, cannot be convincingly explained in this

way. For example the fact that the axonal pathway below the site of injury retains its electrical excitability suggests that the axonal disturbance created by the injury remains localized at the site of damage and is not propagated down the nerve as would be the case if the axon were being deprived and depleted of essential materials. The capacity of a fibre to respond to artificial stimulation is not, however, conclusive proof that the axoplasm has remained unchanged since fibres which will respond readily to artificial stimulation may not conduct impulses which are initiated in the normal way. The fact that the affected axon continues to respond to electrical stimulation by no means excludes the possibility that obstruction to the axoplasmal flow at the site of injury may be a contributing factor in producing the block.

Another finding which it is difficult to reconcile with this concept concerns the transient injury which produces prolonged interruption of conduction. One can visualize an interruption of axoplasmal flow occurring at the time the force is operating but unless a momentary violence causes a more lasting deformation one would expect the flow to be restored before the segment of the axon below the site of injury had suffered severely. Despite this, function is often in abeyance for long periods following injuries induced in this way.

In the present incomplete state of our knowledge we must be content with the explanation that in first degree injury the molecular structure of the axon is temporarily deranged, either by mechanical deformation or ischæmia. The available evidence points to a local disturbance of axoplasmal structure which does not extend distally, rather than to a slowing or arrest of "the centrifugal flow inside the axon of substances or factors vital for the maintenance of axonal integrity." Providing the causative agent ceases to act before the critical point is reached at which axonal disintegration sets in the changes responsible for the block are, whatever their nature, fully reversible and function is rapidly and completely restored.

Observations on the functional disturbances developing as the result of experimentally induced conduction block in human nerves.—There is a growing literature on the effects of compression of human nerves although much of this work, particularly the more recent contributions, has been devoted to a reconsideration of the controversial issues relating to ischæmic and post-ischæmic paræsthesiæ and does not bear directly on the question of conduction block following traumatic nerve injury. Reference will therefore be made only to those observations which are relevant to the subject under discussion.

In 1862 Waller described the effects of compressing the radial, median

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and ulnar nerves in his own arm. The behaviour of limb muscles and nerves during experimental ischæmia was subsequently investigated by Reid (1928) and Lewis, Pickering and Rothschild (1931). With the exception of certain conflicting evidence relating to the initial distribution and mode of spread of the sensory disturbances, later experiments have confirmed the general picture of experimental conduction block as reported by these earlier workers. Despite the fact that cuff compression complicates the picture by rendering the entire limb ischæmic, these experiments can be regarded as having established the following points:

(1) Paralysis and sensory impairment appear fifteen to forty-five minutes after the limb is rendered ischæmic or the nerve is directly compressed (Waller, 1862; Reid, 1928; Lewis *et al.*, 1931; Weddell and Sinclair, 1947; Merrington and Nathan, 1949). Several factors influence the duration of the interval before conduction is blocked but the significant point is that under the conditions of their experiments several minutes of direct pressure and ischæmia were required to effect the block. Lewis *et al.* claim that the onset of paralysis and anæsthesia is delayed for longer periods after direct pressure than after cuff compression but Sinclair (1948) reported that, following direct pressure, anæsthesia "occasionally appeared earlier than in the case of cuff compressions."

(2) Function is rapidly restored following release from pressure which has rendered the limb ischæmic for thirty to forty minutes. Reid reported full motor recovery ten to twelve minutes after cuff compression for an unspecified period which, however, exceeded twenty-five to thirty minutes. In Lewis, Pickering and Rothschild's experiments sensation was fully restored twenty-five to fifty seconds following ischæmia of about twenty-five to thirty-five minutes' duration whereas motor function did not recover fully until seventeen minutes had elapsed. In another series of experiments they found that after thirty-five to forty minutes' compression it took some hours before recovery was complete. Merrington and Nathan, however, reported full motor and sensory recovery within a minute of restoring the circulation after thirty minutes' compression. In Waller's experiments the nerve was directly compressed for forty-five minutes and, though signs of sensory and motor recovery were evident within three minutes after release, recovery was not complete until twelve days later. According to Gasser (1935) "Blockade by compression is only slightly reversible, while fibers blocked under a sphygmomanometer cuff are restored within two minutes after being released from pressure."

(3) Ischæmia of the compressed segment of the nerve is generally held to be responsible for the temporary interference with conduction (Lewis *et al.*, 1931; Weddell and Sinclair, 1947; Merrington and Nathan,

1949). For reasons already detailed this view may need to be revised as regards certain injuries in which mechanical deformation is more likely to be the essential mechanism underlying the production of the block.

(4) According to Magladery, McDougal and Stoll (1950) "marked sensory impairment always appeared long before any perceptible deterioration in motor power" and they concluded that motor fibres are less sensitive to ischæmia than sensory fibres. The records of other workers are not sufficiently complete to determine whether or not they are in agreement with this conclusion. According to Waller the sensory symptoms are those first perceived. Lewis, Pickering and Rothschild report that sensation was impaired before paralysis appeared but whether this preceded the first signs of failing motor function was not stated nor is it clear from their data; following restoration of the circulation, however, sensation recovered in advance of motor function. Other evidence, however, indicates that sensory fibres are more resistant to pressure than motor fibres (Lüderitz, 1881; Gasser and Erlanger, 1929; Denny-Brown and Brenner, 1944*b*). Though the question of relative susceptibility remains unsettled there is no doubt that motor and sensory fibres behave differently; it is the precise manner in which they do so which requires clarification.

(5) The different sensory modalities do not fail simultaneously but are lost in the following order: proprioceptor, touch, temperature and pain sensibility (Herzen, 1886; Goldscheider, 1886; Fabritius and Bermann, 1913; Lewis *et al.*, 1931; Gasser, 1935); Sinclair (1948) has recently shown that "skin touch" fails before "hair touch." In the belief that motor, touch, pain and sympathetic functions were represented in that order by fibres of descending grades of calibre and knowing that the various functions succumbed in the order indicated, Lewis, Pickering and Rothschild (1931) suggested a possible relationship between the survival time of fibres and their size, the larger being more vulnerable than the finer. This argument was invalidated when the fibres subserving the different modalities were shown to be widely distributed throughout the various fibre sizes (Gasser, 1935) and there seems to be little possibility of associating the survival time of the different modalities with differences in fibre size (Gasser, 1935; Lewis and Pochin, 1938; Frankenhaeuser, 1949).

(6) Lewis, Pickering and Rothschild interpreted their findings as demonstrating that a nerve is more sensitive to ischæmia at proximal than at distal levels and that long nerves are affected earlier than short nerves. These interpretations have been criticized by some and supported by others and are still the subject of debate.

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Clinical Features Associated With First Degree Injury

(1) *The nature of the peripheral defect.—(a) Motor and sensory functions:* Motor function is lost and joint sensibility is affected. Both are frequently observed in the absence of disturbances of the remaining modalities of sensation and sympathetic activity. Where fibres subserving sensations other than proprioception are involved, touch is usually affected to a greater extent than pain while both are less severely affected and recover more rapidly than motor and proprioceptor functions. In fact such sensory defects are often so transitory that they are rarely evident unless the patient is examined immediately following or soon after the injury. By the time he presents for examination the only residual sensory disturbance, other than the proprioceptor defect, may be one of paræsthesiæ which subsequently subside. This explains the dissociated loss which is so commonly observed clinically. Sympathetic fibres are the most resistant to this form of injury and if affected they are the first to recover.

It should be remembered that in some cases the condition may be arrested on the verge of paralysis by the removal of the causative agent so that only a paresis results. Such paresis could be due to the maximal involvement of a small number of the nerve fibres innervating a muscle or to the partial involvement of all or a large number of them. The co-existence in any given case of normal, paresed and paralysed muscles appears to be best explained, in terms of our present incomplete knowledge, on the basis of individual variations of susceptibility among motor fibres themselves and to the fact that some occupy more protected positions in the nerve than others.

Explanation of the dissociated functional loss: The dissociated functional loss has not been accounted for satisfactorily. The preservation of normal sensation in the presence of well-established paralysis, which is such a striking feature in many of these cases, is in marked contrast to the experimental pressure effects reported by Waller (1862), Zederbaum (1883), Ducceschi (1901), Lewis, Pickering and Rothschild (1931) and Magladery, McDougal and Stoll (1950). It is in keeping with other experimental observations that sensory fibres are more resistant to pressure than motor fibres (Lüderitz, 1881; Gasser and Erlanger, 1929; Denny-Brown and Brenner, 1944*b*). Clinical observation has, however, convincingly demonstrated that in first degree injuries motor and proprioceptor fibres are more vulnerable than those which subserve sympathetic functions and sensations of pain and touch.

The dissociation cannot be explained solely in terms of varying degrees of mechanical deformation since the violence responsible for a first degree

injury without sensory impairment often exceeds that employed experimentally where disturbances of sensation are recorded. The position of the different fibres in the nerve trunk is also of questionable significance though this factor may influence the differential susceptibility to pressure of some fibres. Thus the escape of the posterior cutaneous nerve of the forearm in first degree compression injuries of the radial nerve is probably due to the separate and protected course normally taken by this branch at the site of compression. The escape of the superficial radial nerve fibres cannot, however, be explained in this manner since they are contained within the main trunk at the point where the latter is compressed. Again, the suggested relationship between fibre size and relative susceptibility in which nerve fibres fail in order of their size has already been shown to be unreliable. In the absence of a satisfactory answer to this question we are compelled to conclude that the resistance of the sensory fibres must be due to some as yet unrecognized property which renders them less susceptible to pressure and ischæmia. In this connexion it is interesting to note that Denny-Brown and Brenner (1944*b*) concluded, on the basis of their observations, that the dissociation is due "to a functional property of the disorder of the axoplasm." If this be the sole explanation, however, how is the early impairment of sensation in the experimental work to be accounted for? (Waller, 1862; Lewis, Pickering and Rothschild, 1931; Magladery, McDougal and Stoll, 1950).

(*b*) *Electrical Reactions:* The electrical excitability of the nerve below the site of involvement and of the paralysed muscles is retained because axonal continuity is preserved and the axonal disturbance responsible for the block of conduction is apparently confined to the site of injury.

(*c*) *Wasting:* Particular interest attaches to the condition of the limb as regards wasting in view of the statement by Denny-Brown and Brenner (1944*a*) that "anatomic continuity of nerve, not receipt of impulses, prevents atrophy and fibrillation of muscle."

Recovery may commence too early and advance too rapidly for wasting to make an appearance. Wasting, however, is present in those cases in which the onset and progress of recovery are delayed though the delay is never great enough to permit wasting to reach the degree observed after nerve severance. Lest the atrophy be attributed to disuse of the affected limb it should be pointed out that the wasting is maximal in the involved muscles even if it is not entirely confined to them. Furthermore it improves only with the onset of recovery and its disappearance closely parallels the return of power in the affected muscles.

(2) *The duration of loss of function.*—The onset of recovery in the paralysed muscles is delayed for periods ranging from a few minutes to

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several weeks (sixty days in the author's experience) though only in the exceptional case is it delayed beyond the fourth week. What is the explanation of the variation in the duration of the interval elapsing between the infliction of the injury and the onset of recovery? Persistent constriction, which is sufficient to block conduction but insufficient to threaten axonal continuity, may be a factor in those cases in which neurolysis is rapidly followed by recovery which reappears in such a way as to exclude the regeneration of axons. There remains those cases in which a paralysis of variable duration is associated with causative injuries which appear to be of comparable severity. In their experiments Denny-Brown and Brenner (1944*a*) were unable to establish any relation between the duration of the paralysis and either the pressure employed to induce it or the time for which it was applied. There seems little doubt that variations in the severity of the axonal changes must be responsible but since we are ignorant of the nature of the change itself it would be idle to speculate on possible variations which would account for the fact that in some individuals the muscles remain paralysed for longer periods than in others. To attempt to explain this phenomenon on the basis that the injury sustained in one case is more severe than that in another does not increase our understanding of the problem.

Cutaneous sensory loss is usually transient; touch, which is affected to a greater extent than pain, recovers more slowly. Paræsthesiæ indicative of disturbed conduction may persist for several days. In comparison the onset of recovery in proprioceptor mechanisms is delayed.

(3) *The course of recovery.*—After a quiescent period of variable duration the pathways suddenly reawaken to activity. Cutaneous sensation recovers well in advance of motor and proprioceptor functions and so rapidly that by the time the patient comes under treatment the opportunity to study the way in which it does so has passed.

More information is available concerning the manner in which function is restored in the affected muscles.

(*a*) Recovery may appear simultaneously in muscles in which the nerve-fibre length from the site of injury differs greatly.

(*b*) There is no orderly progress of regeneration down the nerve with the reinnervation of muscles determined by the site of origin and length of their branches. On the contrary the site of the first appearance of recovery varies and on occasions more distally supplied muscles recover slightly in advance of those innervated at a higher level.

(*c*) Keeping in mind the fact that frequently two or more muscles commence to contract simultaneously, it has been observed that once conduction reappears in one muscle there is only a short interval before all muscles supplied by the nerve are contracting.

(*d*) Recovery which soon reappears either simultaneously in all the affected muscles or extends so rapidly as to involve them all cannot be accounted for by the regeneration of axons following Wallerian degeneration.

(*e*) The first muscles to contract are not necessarily the first to recover their power completely. This lag in restoration of power, as distinct from the time of appearance of contraction, together with differences in the time required to effect recovery in the various muscles, can best be explained in terms of the severity of the injury sustained by individual nerve fibres to the same and different muscles.

(4) *The end-result.*—Complete restoration of function inevitably follows this type of injury since axonal continuity is preserved and the changes responsible for the interruption of conduction are fully reversible. A residual defect indicates a loss of axons or a disturbance of the pattern of innervation and these are complications which can only occur with more severe degrees of injury.

(5) *The period required to effect complete restoration of function.*—Dynamometer and spring-balance reading of muscle action indicate that full restoration of function may be delayed for three to four months after the injury and in exceptional cases for six months.

Second Degree Injury

In a second degree injury the axon is severed or axonal mechanisms are so disorganized that the axon fails to survive below the level of the injury and perhaps for a short distance proximal to it. The general arrangement of the axon sheaths and remaining structures comprising the nerve is preserved and the reaction which develops as the result of the injury and the ensuing Wallerian degeneration does not threaten the integrity of the endoneurial tubes.

Disintegration of the axon is accompanied by the breakdown of its myelin sheath. As a result of these changes and the associated Schwann cell and phagocytic activity the contents of the endoneurial tubes fluctuate in both quantity and composition throughout the various phases of degeneration but ultimately they are entirely the products of Schwann cell proliferation. In this way the peripheral end-organ becomes isolated from its corresponding neuron and axonal continuity between the two must be restored before recovery can occur. This is effected by the regeneration of the intact portion of the axon which, after a delay of a few days, commences to grow distally. In its advance the axon is confined to the endoneurial tube originally occupied by it and in this way is prevented from reaching and descending along foreign tubes. This ensures that the axon is inevitably directed back to the end-organ which it

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originally innervated. The fibre pattern following reinnervation is consequently identical with that obtaining before the injury with the result that function is fully restored.

Clinical Features Associated with Second Degree Injury

(1) *The nature of the peripheral defect.*—There is complete loss of motor, sensory and sympathetic functions in the autonomous distribution of the injured nerve. Axonal degeneration is complete by the ninetieth hour after the injury. Subsequent to this the involved section of the nerve does not respond to electrical stimulation while the affected muscles atrophy and show the typical reaction of degeneration.

(2) *The duration of loss of function.*—The latent period elapsing between the infliction of the injury and the onset of recovery comprises: (i) the quiescent period before the axon tips commence to regenerate and (ii) the time taken to regenerate functionally efficient pathways which in turn involves: (*a*) the re-establishment of axonal continuity; (*b*) changes in the structure of the regenerated fibre, defined as maturation, which lead to its functional efficiency as a conducting pathway; (*c*) analogous changes at the end-organ leading to effective union with muscle fibres and skin; and (*d*) a minimum number of mature fibres which must be present before voluntary contractions appear.

The duration of the latent period is influenced by such factors as the level of the injury, the rate of advance of axon tips, and the duration of denervation of the affected tissues. Each of these presents individual variations but they all combine to make the latent period much longer than after first degree injury. This feature has been discussed in detail elsewhere (Sunderland, 1947).

(3) *The course of recovery.*—Since recovery depends, *inter alia*, on the restoration of axonal continuity the pattern of recovery after this type of injury differs significantly from that occurring after first degree injury. In the latter motor function reappears simultaneously, or almost so, over the entire field. After a second degree injury the affected muscles are reinnervated in the order in which they were originally supplied so that the onset of recovery in individual muscles proceeds in serial order from above downwards, the proximally supplied muscles recovering before those innervated at more distal levels.

Since the sensory fibres degenerate and regenerate as do the motor fibres, and presumably in much the same way, the onset of sensory recovery will be in strict conformity with the distance which must be grown by the sensory processes. The possibility remains, however, that regenerating sensory dendrites may advance more rapidly than motor axons though there is no information on this point.

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Hoffman-Tinel's sign: The descent of regenerating sensory dendrites can often be followed down the nerve by tracing the progression of the point at which Hoffman-Tinel's sign can be elicited. The progress of this sign is a reliable guide to recovery in this particular type of injury because the sensory dendrites are descending in their original tubes and the pattern of sensory innervation is ultimately fully reconstituted.

(4) *The end-result.*—Function is completely restored since the fibre pattern following reinnervation is identical with that obtaining before the injury. In the exceptional case there may be a very mild residual functional defect which can be due only to a retrograde degeneration which reduces the number of the axons. This, however, rarely occurs with an injury which leaves all but the axons of the nerve intact.

(5) *The time required to effect complete restoration of function.*—Owing to the factors which delay the onset of recovery and its extension to the entire peripheral field the time required to effect complete recovery exceeds that required after a first degree injury.

Third Degree Injury

A third degree injury results from more severe trauma which, in addition to causing axonal disintegration and Wallerian degeneration, disorganizes the internal structure of the funiculi. Although the tissues comprising the perineurium may show minor changes the general arrangement is retained so that the bundles remain in continuity and show little, if any, deformation of their outlines. The essential change is therefore a disorganization of the internal structure of the bundle in which endoneurial tube continuity is lost. In the more severe forms of injury the picture of fibre disorganization is further complicated by intrafunicular hæmorrhage, œdema, vascular stasis and ischæmia. These complications all favour the development of an intrafunicular fibrosis which provides the most serious obstacle to regeneration.

Degeneration follows the same pattern as that recorded for a second degree injury but regeneration is now complicated by the intrafunicular damage. Firstly, the retrograde effects are likely to be more severe after such injuries, particularly when these are sustained at proximal levels. This delays the onset of regeneration in units which must first recover from retrograde changes and where these changes have progressed to degeneration there is a consequent reduction in the number of axons available for regeneration. Secondly, the regeneration of axons is complicated by the presence of any intrafunicular fibrosis which obstructs or diverts them from their proper paths and, later, by constricting them, adversely affects conduction. In some cases these complications may be

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so pronounced that the involved funiculus develops a fusiform swelling. Thirdly, loss of continuity of the endoneurial tubes means that regenerating axons, though still confined within the funiculi, are no longer confined to the tubes which originally contained them. Since there is no known mechanism which ensures that the axons will seek out and enter their old tubes they are now free to compete for the tubes below the lesion. This competition is aggravated by such factors as (*a*) the axonal sprouting which occurs during regeneration and which results in an excess of axons over endoneurial tubes owing to the fact that there is no multiplication of the latter, and (*b*) the deflection of axons from their proper course by fibrous tissue. Many axons consequently fail to descend along their original or functionally related tubes but are, instead, misdirected into foreign tubes. The pattern of reinnervation is thereby considerably modified.

Thus after a third degree injury some axons are irreparably lost as the result of retrograde neuronal degeneration while others are prevented from growing distally by the fibrous obstacle interposed in their path. The adverse effects of the erroneous cross-shunting require further consideration since these effects are influenced by the fibre composition of the injured funiculus.

Attention has already been directed to the fact that funiculi are of two types depending on their fibre composition: both types occur together at the same level. The first type is composed solely of fibres from one branch while the second contains fibres from several sources in varying combination and proportions. The consequences of intrafunicular damage rupturing the endoneurial tubes are not the same in each case. Where a funiculus contains fibres from one, or two functionally related sources, e.g. the radial extensor muscles of the wrist, it is of little moment if fibre mixing does occur since the regenerating axons are confined within the funiculus and all routes lead to the same or a functionally related tissue. Under these conditions they may not reach their original end-organs but must reach ones which are functionally related. Where, on the other hand, the funiculi are composed of intermingled fibres from several different and functionally unrelated sources, the entry of axons into foreign tubes will distort the fibre pattern and in this way seriously impair the functional efficiency of regeneration despite the fact that the injured funiculi are in continuity. The consequences of a distortion of the fibre pattern arising in this way are particularly serious when all the fibres are contained in one or two large funiculi as is the case at certain levels in some specimens of some peripheral nerves (e.g. ulnar, radial, lateral popliteal and axillary). Under these conditions the chances of erroneous cross-shunting of axons into foreign tubes are multiplied and the new fibre pattern may be so distorted in comparison with the old that little recovery

may result despite the fact that funicular continuity is preserved with no external indication of the severity of the intrafunicular damage other than perhaps some slight swelling and induration. The existence of numerous small funiculi at least restricts the influence of these factors to small and separate groups of fibres rather than to one or two large groups but the result will be the same if all the bundles are involved simultaneously and to the same degree though this is less likely to occur than when the nerve is composed of a single bundle.

We have already observed that at proximal levels the fibres from the most distal structures are intermingled and widely distributed over the funiculi whereas the fibres from branches of high origin are more discretely localized. It therefore follows that in high lesions the consequences of an injury that ruptures the endoneurial tubes and produces fibre mixing are more serious for distally innervated structures than they are for the proximally innervated structures. In this way the level of the lesion becomes a factor influencing the extent and quality of the recovery.

The effect of partial lesions is determined by the fibre composition of the involved funiculi. If these contain a proportion of the fibres from each of several sources there will result a widely distributed paresis and/or sensory impairment. On the other hand, if they contain all the fibres destined for a particular muscle or muscles or cutaneous area the result will be a sharply localized paralysis and/or discrete area of sensory loss.

Details of the fibre composition of the funiculi at various levels for the different peripheral nerves have been given elsewhere (Sunderland, 1945; Sunderland and Ray, 1948). This information is important because it provides the clue to the profound peripheral effects and the poor results which sometimes follow lesions in continuity in which there are no obvious signs of damage.

Clinical Features Associated with Third Degree Injury

(1) *The nature of the peripheral defect.*—When the intrafunicular damage involves all the bundles there is complete loss of motor, sensory and sympathetic functions in the field served by the nerve. For reasons detailed in the previous section the nature of the peripheral defect in partial lesions depends on the fibre composition of the involved funiculi. This defect may range from a widely distributed paresis and/or sensory impairment to a sharply localized paralysis and/or discrete area of sensory loss.

(2) *The duration of loss of function.*—The onset of recovery is delayed for longer periods after third degree than after second degree injury. This is due to (*a*) the more severe retrograde disturbances which are corrected

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more slowly, (*b*) the additional time taken by regenerating axon tips to penetrate any fibrous tissue which slows them, and (*c*) the delayed reinnervation of the peripheral apparatus consequent on (*a*) and (*b*) which prolongs the time taken to restore functional end-organ relationships following the re-establishment of axonal continuity.

(3) *The course of recovery.*—This is substantially the same as that observed after a second degree injury. There is usually the same serial order of reinnervation but this may be modified slightly owing to the fact that some regenerating axons are delayed longer than others by scar tissue at the site of injury. Third degree injuries, however, differ in the following respects. Recovery in individual structures takes place more slowly and is usually incomplete, a paresis and/or sensory defect remaining to indicate the disturbance of the pattern of reinnervation occurring during regeneration and the loss of axons from retrograde degeneration. The recovery in some structures is better than in others, depending on the fate of the axons originally innervating them. The muscles which recover fully often take longer to do so. The following factors contribute to the slower recovery.

(*a*) The duration of denervation is longer and this may be responsible for introducing changes of an intramuscular character which delay the full restoration of function following reinnervation.

(*b*) Fibre mixing at the site of injury may so distort the normal pattern of innervation as to render it temporarily less efficient but not to a degree as to prevent full compensation by re-education. Such correction, however, requires additional time and delays recovery.

(*c*) Some muscle fibres may not be reinnervated owing to the number of surviving neurons becoming depleted as the result of retrograde degeneration and the failure of some regenerating axons to reach the muscle. This loss may be offset by the "use" hypertrophy of those fibres which have fully recovered but this process also lengthens the time required to effect complete restoration of function.

Hoffman-Tinel's sign: Once the endoneurial tubes have been ruptured and regenerating axons are free to enter foreign tubes Hoffman-Tinel's sign ceases to be a guide to the quality of the recovery. Though indicating the presence and descent of regenerating sensory processes the sign gives no information as to whether or not erroneous cross-shunting has led them into motor tubes.

(4) *The end-result.*—There is a residual defect which varies in degree depending on the axon loss and the erroneous cross-shunting at the site of injury.

Fourth Degree Injury

A fourth degree injury is one in which the entire funiculus is involved, all bundles being breached and so disorganized that they are no longer sharply demarcated from the epineurium in which they are embedded and which shares in the reaction. Continuity of the nerve trunk is, however, preserved but the involved segment is ultimately converted into a strand of tissue composed of a tangled mass of connective tissue, Schwann cells and regenerating axons which may be enlarged to form a neuroma. Wallerian degeneration occurs as in the second and third degree injury but regeneration is still further complicated in comparison with these.

(*a*) The retrograde neuronal effects are more severe following an injury which ruptures the funiculi. There is a high incidence of degeneration and a correspondingly greater reduction in the number of surviving axons.

(*b*) The regenerating axons, instead of being confined to the funiculi, are left free to enter the interfunicular spaces. As a result many fail to establish contact with the endoneuronial tubes below the site of destruction. Because of the free wandering of regenerating axons which occurs in the injured segment many become lost and terminate blindly while the chances of others entering foreign tubes are greatly increased.

(*c*) Scarring is more severe when the endoneurium, perineurium and epineurium have been damaged. The disorganized nature of the tissue, its density and its wide distribution through the nerve aggravate the axonal loss and erroneous cross-shunting.

Clinical Features Associated with Fourth Degree Injury

When all the funiculi are involved there is complete loss of motor, sensory and sympathetic functions in the field served by the nerve. The nature of the peripheral disturbance in partial fourth degree injuries depends, as in third degree injury, on the fibre composition of the involved funiculi.

As in third degree injuries factors are present which retard and complicate regeneration but in the case of funicular disorganization they are far more serious. The retrograde effects are more severe, large numbers of regenerating axons escape into the interfunicular connective tissue spaces and never reach the periphery while others are directed into functionally unrelated endoneurial tubes. Though some spontaneous recovery occurs it rarely proceeds to a useful degree. This is the type of injury which requires excision of the involved segment and surgical repair of the nerve.

Fifth Degree Injury

A fifth degree injury implies loss of continuity of the nerve trunk which results in the complete loss of motor, sensory and sympathetic

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functions in the autonomous distribution of the severed nerve. The extent of the separation of the nerve ends varies. The appearance of the involved nerve depends on the time when the injured region is examined since the reaction developing at the site of the injury and the subsequent regeneration modify the picture. In general either one or other of the following arrangements will be found. Either the nerve ends will remain separated or they will be joined by an attenuated strand of tissue composed of a fibroblastic and Schwann cell framework transmitting regenerating axons. The latter arrangement is seen only after a sufficient time has elapsed to enable the neural, Schwann cell and fibroblastic activity to bridge the gap. Bulb formation can occur on the proximal stump, the distal stump, or on both.

Wallerian degeneration occurs in the distal segment. Though some regenerating axons may reach and descend along the distal stump to reinnervate the periphery such spontaneous recovery is usually of little value because the axons are few in number and the chances of restoring functionally useful end-organ connexions are very slender indeed. Some of these axons may give a Hoffman-Tinel's sign. It is therefore apparent that the presence of the sign is an unreliable guide to the nature of the injury and the quality of the end-result.

Recovery after an untreated fifth degree injury is reduced to a negligible level owing to a combination of factors.

(1) The retrograde neuronal effects are severe; there is a high incidence of degeneration and consequently a greater reduction in the number of surviving axons.

(2) The majority of the regenerating axons fail to reach the funiculi and the endoneurial tubes of the distal stump owing to:

(*a*) The separation of the nerve ends. Even when the ends are close together large numbers of regenerating axons escape into the intervening tissue as they emerge from the open end of the proximal stump. This wasteful regeneration is increased as the distance between the nerve ends increases.

(*b*) The dissimilarity of the cross sectional area of the nerve ends consequent on denervation shrinkage of the distal stump which increases with the period of denervation (Sunderland and Bradley, 1950).

(*c*) The dissimilarity in the funicular patterns of the nerve ends which becomes a serious factor when there is loss of tissue. The funicular pattern of the nerve ends will only correspond in every respect after clean severance (Sunderland, 1945).

(*d*) The scarring between the nerve ends which obstructs axons and favours erroneous cross-shunting.

The chances of restoring useful connexions are, of course, greatly aided by suturing the nerve ends but despite this there still occurs a significant loss of axons and distortion of the fibre pattern. A consideration of the several factors influencing the extent and quality of the recovery after repair does not fall within the scope of the present paper and will be treated separately. However several factors, some of which have already been mentioned, combine to affect recovery adversely and these are of such an order that, even in the most favourable cases of repair, complète restoration of function is impossible.

Partial and Mixed Injuries

Some fibres in the nerve may escape involvement while others sustain a variable degree of damage. The nature of the peripheral defect, the course of recovery and the end-result depend on the particular fibres involved and the particular type of injury sustained by each.

However in injuries as severe as partial severance and partial fourth degree involvement it is unlikely that the remaining fibres in the nerve will escape some injury. The condition would then be more properly classed as a mixed lesion in which all the fibres were affected to a varying degree.

It is obvious from the classification that fourth and fifth degree injuries (where *all* parts of the nerve are crushed or severed respectively) cannot co-exist either together or in combination with any of the minor degrees of injury. However it is possible for partial severance or subtotal fourth degree involvement of the bundles to co-exist with minor degrees of injury to the remaining fibres of the nerve. Furthermore within bundles surviving in continuity it is possible to meet with every grade of intrafunicular damage ranging from a first degree injury to one in which intrafunicular disorganization leads to destruction of the endoneurial tubes.

Such mixed lesions result in the complete loss of motor, sensory and sympathetic functions in the autonomous distribution of the injured nerve. Since the damage falls unevenly across the nerve so that some parts are more severely affected than others, the duration of the loss of function, the course of the recovery and the end-result will depend on the relative extent of each type of injury and the particular injury sustained by individual fibres. In this way partial and combined lesions can be explained in terms of the five primary types outlined.

Summary

A classification of peripheral nerve injury has been advocated which is based on the extent of the damage to the normal anatomy of the nerve trunk. Five degrees of injury, in ascending grades of severity, have been

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defined. These affect successively conductivity, the continuity of the axon, the endoneurial tube and its contents, the funiculus and its contents and finally continuity of the nerve trunk.

(1) *First degree injury.*—Conduction is blocked at the site of injury but the continuity of all components comprising the nerve trunk, including the axon, is preserved. There is no Wallerian degeneration and the disturbance which is responsible for blocking conduction is fully reversible. After a dormant period the nerve fibres reawaken to activity. The affected parts commence to function either simultaneously or within a very brief interval of one another. Function is rapidly and completely restored. The fundamental basis of this injury is therefore interruption of conduction with preservation of anatomical continuity.

(2) *Second degree injury.*—Here disintegration of the axon and all the associated changes collectively referred to as Wallerian degeneration occur below the site of the injury and perhaps for a short distance above it. The general arrangement of the axon sheaths and the remaining structures comprising the nerve is preserved and at no time is the integrity of the endoneurial tube threatened. Axonal connexion with the periphery is restored by the regeneration of the intact portion of the axon. In its advance the axon tip is confined to the endoneurial tube originally occupied by the axon and this ensures that the axon is inevitably directed back to the end-organ which it originally innervated. The fibre pattern following reinnervation is consequently identical with that obtaining before the injury so that function is fully restored. Since recovery depends on the regrowth of the axon, structures recover in the order in which they were innervated.

The fundamental basis of a second degree injury is disentegration of the axons which subsequently regenerate. Owing to the preservation of the endoneurial tubes this regeneration results in the complete restoration of the original pattern of innervation.

(3) *Third degree injury.*—The internal structure of the funiculi is disorganized though the bundles remain in continuity and show little, if any, deformation of their outlines. In addition to axonal disintegration and Wallerian degeneration, continuity of the endoneurial tubes is also destroyed. Disorganization of the internal architecture of the funiculus complicates regeneration by fostering intrafunicular fibrosis while regenerating axons, though still confined within the funiculus, are no longer confined to the endoneurial tubes which originally contained them. As a result axons are obstructed in their growth and may be misdirected into foreign tubes so that the pattern of reinnervation may be considerably modified. The adverse effects of erroneous cross-shunting of axons vary

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with the fibre composition of the individual funiculi, being greater when the bundles are composed of intermingled fibres from several different sources than when they are composed of fibres from the same branch.

The fundamental basis of a third degree injury is the disorganization of the contents of the funiculi so that the continuity of endoneurial tubes is destroyed and the chances of erroneous cross-shunting of regenerating axons are introduced.

(4) *Fourth degree injury.*—Here the funiculi are breached and disorganized so that they are no longer sharply demarcated from the epineurium in which they are embedded. Continuity of the nerve trunk is preserved, however, the involved segment being ultimately converted into a strand of tissue composed of a tangled mass of connective tissue, Schwann cells and regenerating axons which may become enlarged to form a neuroma. After such an injury regenerating axons are left free to enter the interfunicular spaces. Because of the free wandering of regenerating axons which occurs at the site of injury many become lost and terminate blindly while the chances of others entering foreign tubes are greatly increased. There is also a more severe fibrous tissue reaction after a fourth degree injury and this aggravates the axonal loss and erroneous cross-hunting. The fundamental basis of a fourth degree injury is complete disorganization of the internal structure of the nerve with preservation of continuity.

(5) *Fifth degree injury.*—The fundamental basis of a fifth degree injury is severance of the nerve trunk.

(6) The clinical features associated with each type of injury have been discussed.

(7) Partial and mixed lesions can be explained in terms of the five primary types outlined.

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Notices of Recent Publications

Wisdom, Madness and Folly. By John Custance. Introduction by Canon I. W. Grensted. 1951. Pp. 354. London: Victor Gollancz Ltd. Price 16s.

The author has had several attacks of mania and depression and devotes the first part of his book to describing these states, the second part to an attempt to synthesize the totality of his experiences, normal and abnormal, in a coherent philosophy. The basic assumption, that from a philosophical point of view abnormal mental experiences are as valid as normal ones, must be conceded. The question remains whether they are to be regarded as real in the same way. The author adopts a philosophical system of an idealist type, which he calls the Theory of Actuality, in which no distinction of principle is drawn between hallucinatory and normal perceptual experiences. Jungian psychiatry and the concept of the collective unconscious provide a very convenient framework. The objection can, however, be made that the physical bases of a hallucinatory and a normal perceptual experience are different, and that while the latter can provide self-consistent information about the world outside the subject, the former cannot. It does not appear to the reviewer that this objection is adequately dealt with. The main objection to idealist philosophies such as that proposed by Mr. Custance is not that they are illogical but that they are dead ends heuristically.

The book is of more than usual interest to psychiatrists, and probably also to philosophers and theologians. The self-descriptions are painfully vivid, the philosophical argument is enriched by a mass of curious learning, and the engaging personality of an original writer illumines the whole. T. E. S.

Lebenserinnerungen. By Julius Wagner-Jauregg. Edited by L. Schönbauer and M. Jantsch. 1950. Pp. x+187: 46 Illustrations. Vienna: Springer-Verlag. Price, paper covers 17s., bound 20s. 6d.

Wagner-Jauregg died at the age of 83, and spent the last year of his life in writing an autobiographical sketch. This was not intended for general publication, but for circulation in the family and among colleagues and friends. When the manuscript came into the hands of the senior editor, however, he considered that it was of sufficient interest for publication. The manuscript has been in part rearranged and has been substantially added to. The three chapters devoted to Wagner-Jauregg's main achievements, the reform of the lunacy laws in Austria, the prevention of goitre, and the malarial therapy of general paresis, have been separated out from the main thread of the life story and supplemented by historical introductions and other explanatory passages by the editors. The distinction between Wagner-Jauregg's own text and that of the editors has been clearly made; and these supplements are very useful. The illustrations, mostly portrait photos of the teachers and colleagues mentioned in the text, are also a valuable addition.

Reading the main text, one is struck with wonder that a man of 82 could have written with such vigour and coherence; the style is that of a man in his prime. The accounts of student days, of his first Professorship in Graz, and of

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the great part of his life which was spent in Vienna, are all told with great objectivity, and keep closely to the facts. One misses any description of his private life, and the emotional side of his professional activities, his doubts and hesitations, his disappointments and moments of triumph, must be largely read between the lines. There is, for one of the world's greatest psychiatrists, very little in the way of descriptions of personalities, either of his friends or enemies. Nevertheless, the picture which emerges is full of interest. The events themselves in which he was involved were full of colour, and gain by his terse, vigorous and objective description. One learns, for instance, what immense importance was attached in Vienna, seventy years ago, to the Professor's "Vorlesung," that Bamberger gave lectures rich in content and perfect in form, but seemed to be bored by the whole affair; but that Stricker laid the greatest emphasis on being *en rapport* with his audience, and for that purpose took lessons from a famous actor. Stricker, also, carried out experimental operations in the lecture theatre, so that his lectures were very popular. Before his day few medical men had ever seen a beating heart, unless with luck that of a frog.

Wagner-Jauregg himself must have been a towering personality. The several photographs which are reproduced show a face built on massive and rugged lines, determined to the point of sternness, a Chief and teacher who would be awe-inspiring. He would seem to have been a loyal friend and an enemy to be feared. Not once but several times he fought his opponents in energetic polemic, apparently always with justice on his side. These debates were never about trifles, but matters of principal importance. The purely human side, of which one would have liked to read more appears but seldom in his self-description. In 1924 he learned that he would receive the Nobel prize, but would have to wait till 1927. Gadelius, one of the referees, had reported that a man who could inflict malaria on a patient already suffering from paresis, so far from deserving the Nobel prize, was in his eyes a criminal. Wagner-Jauregg would have to wait three years till Gadelius had been pensioned off. In 1927, however, in a list of Nobel candidates published in the Press Wagner-Jauregg failed to find his name, and accepted this with resignation. One night in September he was rung up by a Berlin reporter to enquire whether he knew whether he was among the candidates. About eleven that night the same correspondent telephoned again to say that the Karoline Institute was still in session, the result unknown. Once more Wagner-Jauregg composed himself to sleep. Finally he was woken again at 1 a.m. by the same man, to say that he had just been awarded the prize. Then at last there was an end of sleep. He rose and played chess with himself until the official announcement arrived in the early morning.

The malaria story is full of interest. The earliest experiments were made with all kinds of psychotic patients, and with all sorts of methods of causing fever. For a long time he worked with injections of tuberculin, and got some very promising results, which, however, when presented to the International Medical Congress in 1909 met with scepticism and hardly aroused discussion. When he eventually came to work with malaria, he could have learned little from our modern ideas of statistics—choosing patients from the admission list alternately for treatment and for control. The Nobel prize was well earned. Not only did he provide a specific cure for a deadly scourge, but he had won success by his own insight, his scientific honesty, his energy and dauntless perseverance. T. E. S

Les Hallucinations. Clinique et Biologie. By JEAN LHERMITTE. 1951. Pp. 230. G. Doin & Cie. Editeurs, Paris (VIe). 930 fr.

This book is not so much an exhaustive or encyclopædic account of perceptual disorders, as a selective essay upon those aspects of the problem of hallucinations which have most interested the writer. It is not surprising, therefore, that the

most arresting chapters are those dealing with peduncular hallucinosis, phantom limbs and heautoscopy. The last-named topic is studied from many sides, including the data afforded by psychopathology, belletristic literature and even folk-lore. The author has obviously adhered to the *obiter dictum* of Ernest Dupré—". . . Do you seek to probe the secrets of psychiatry? Then study the poets and romantic writers." Of particular value are the introductory pages which are mainly historical in scope, and trace the growth of opinion about sense disorders from the early natural philosophers to the present day. An unexpected and fascinating section deals with the more mystical side of hallucinosis, as evidenced in parapsychical phenomena, diabolism, and sundry delirious manifestations of religious life.

Professor Lhermitte's writings always betray a fundamental learning redeemed by that cultural leavening which is so characteristic of all that is greatest in French neurology. This monograph is typical in that respect. The literary style is distinctive, easy, masterly and rich. M. C.

On Changes in Circulation through the Anterior Cerebral Artery: a Clinico-angiographical Study. By SVEN ETHELBERG. 1951. *Acta Psychiatrica et Neurologica*: Supplementum No. 75. Universitits-forlaget i Aarhus. Pp. 211. Price not stated.

Here the title is scarcely adequate for it gives no indication of the wide range of topics considered. The morphology of the anterior cerebral artery is first described, including the contribution which arteriography has brought to our anatomical knowledge. This technical procedure has enabled the author to consider the vascular deviations which arise in association with aneurysms, angiomata and meningiomata. The radiological appearances of occlusion of the anterior cerebral artery are illustrated by a large number of skiagraphic sketches. Physiological matters are dealt with in a brief and non-committal fashion, the author taking up an equivocal position as regards the uneasy doctrine of suppressor bands. He touches upon the recent work dealing with stimulation of the cingulate gyrus. The second half of the monograph concerns the clinical features of ischæmic lesions in the territory of this artery. A cautious introduction, stating his adherence to the principle of distinguishing lesions from functions, seems, unfortunately, still to be necessary in neurological literature today. The author rightly dislikes the neurosurgical attempts to look upon the anterior cerebral artery of the dominant hemisphere as the "artery of consciousness."

Two thoughtful chapters are included in this section, which are well worth perusal. The one concerns the apraxias and other psychomotor anomalies. The other (Chapter X) is interesting in that it gives a phonetic analysis of the cortical dysarthrias and other speech disorders which may follow occlusion of the anterior cerebral artery. This is a type of investigation which might well be prosecuted more often and in other types of cerebral disease.

The English in which this monograph is written is far better than one usually finds in a Supplementum of the *Acta Psychiatrica et Neurologica.* M. C.

The Post-natal Development of the Human Cerebral Cortex. Volume IV. *The Cortex of the Six-month Infant.* By J. LE ROY CONEL. 1951. Pp. 191 with 108 full page plates. Harvard University Press. (London: Geoffrey Cumberlege). Price 82s. 6d.

The earlier volumes of this series were reviewed in BRAIN in 1939, 1942 and 1948. The present volume is as full of careful observation as these, and the plates are as carefully chosen and reproduced. It describes an orderly development, along

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the lines indicated in the third volume, which dealt with the cortex of the 3-month infant: the projection areas headed by the motor cortex lead the advance, with the association areas following. While there is little, if any, increase in size of the bodies of the nerve cells between 3 and 6 months of age, there is considerable development of Nissl granules and neurofibrils, an increase in the size, length and compactness of the dendrites and, along with this, an increase in the thickness of the cortex especially in the third to fifth layers. The gyri also have become wider and longer, so that the neurons are spaced further apart; this was found throughout the cortex in all layers except the fifth where, in a few association areas, the cells are actually more closely set. Development of neurofibrils has proceeded *pari passu* with increase in chromophil substance. The giant Betz cells are most advanced in both respects in the order of (1) hand area, (2) trunk and arm area, (3) head area and (4) leg area. Next come the other main projection areas PB, PC, OC and TC in that order, with the association areas less advanced. The pyramidal cells of the hippocampus are still devoid of neurofibrils as are also the cells of the granular layers in all areas. Myelination also is proceeding rapidly at this age although not yet completed. It is interesting to learn that it is much further advanced in the brains of well-nourished infants than in that of a marasmic infant of the same age, in which it was scarcely more advanced than in the average 3 months' brain.

The author concludes this important survey by cautioning the reader against the view that such differences in cellular structure as exist between different areas of the cortex indicate differences in function. In his view the structure of the cortex is modified by mechanics and the function of any area is wholly determined by its fibre connexions. J. G. G.

The Neurosurgical Treatment of Traumatic Paraplegia. By J. Lawrence Pool. Springfield, Illinois: Charles C. Thomas.

In this monograph spinal cord injuries are considered along conventional lines. In the space of one hundred pages the pathology and physiology of these injuries, their clinical features, diagnosis and treatment—operative and non-operative—and the management of the paraplegic patient are discussed. While the book should provide a useful introduction to the subject, one is left with the impression that its value could have been greatly enhanced, for example, by the omission of the sections on first-aid treatment and chemotherapy and their replacement by detailed information concerning tidal drainage of the bladder, the indications for laminectomy in these cases, etc. Like other volumes in this series it is beautifully produced and well illustrated.

J. E. A. O'C.

Die Nervenkrankheiten. By Georges Schaltenbrand. 1951. 880 pages, 539 figures. Stuttgart: Thieme Verlag. Price 87 marks.

It is many years since a textbook of neurology of this scope has appeared in the German language. Perhaps the last comparable work was Oppenheim's two volume classic, familiar to English neurologists of the last generation in Bruce's admirable translation, or in the original.

Oppenheim's work was, of course, far more compendious than the book under review, but it included the customary chapters on the anatomy and physiology of the nervous system that Schaltenbrand proposes to deal with in a following volume, the two making together a "Lehrbuch der Neurologie." Nevertheless, Oppenheim gave more space to clinical description, and indeed his book was modelled on Gowers' famous text, which he believed that he had outshone. It is true that his work was more modern and thus included clinico-pathological entities and neuropathological details

not revealed in Gowers' day, but no one familiar with both texts, would have exchanged his Gowers for an Oppenheim. The clinical descriptions in Gowers text, his sense of illness as being a process the course of which it was his business to depict, make his book to this day quite incomparable.

Packed with information, Oppenheim's descriptions had little sense of process, they were not easy to read, and they did not convey the impression of vast clinical experience and sagacity that shine out from Gowers' beautifully written pages.

It is yet a compliment to say that Schaltenbrand's shorter work invites comparison with Oppenheim from anyone who has read that great work, for in style and construction it closely resembles it, with its virtues and its shortcomings. It is difficult to read, not only because too many pages are broken up by illustrations so that the text may be reduced for part or whole of a page to a narrow column of but three or four words to a line—a bad defect of production and not of authorship—but because it is tabular in form rather than descriptive. The reader rarely gets a picture of the maladies dealt with, but he gets a full list of, and commentary upon, the signs and symptoms. Take tabes dorsalis, for example, all the signs are there, but few would gain an adequate impression of the variable course of this malady, and of the differing clinical pictures it presents in different subjects. This criticism applies to all the clinical content of the book. Useful as a reference book, few would want to sit down to read it at large.

It is comprehensive, and what we have described as a defect in the book, arises of course in part from this. When so much is attempted in less than 900 pages, extreme compression is inevitable.

Neuropathology is adequately dealt with, and like the clinical accounts is copiously and well illustrated by half-tone plates.

An effort has been made to bring the book up to date. For example, there is a brief—if wholly unexplained—reference to the association of immunizing inoculations with paralysis in poliomyelitis, but in very many most important respects the work is out of date.

The section on the treatment of neurosyphilis might have been written ten years ago, and the role of penicillin is sketchily dealt with in a useless paragraph that gives no clue to modern experience and practice, while a page is devoted to mercurial inunction in combination with potassium iodide. Sciatica is found amongst the "rheumatic neuritides" and treated by a battery of long-discarded remedies and procedures, while its association with herniation of lumbar intervertebral discs finds casual mention in another chapter of the book. The thoracic inlet syndrome is dismissed in a paragraph. The discussion on the ætiology of polyneuritis is quite out of date and might have been taken from a text of the last generation, also inadequately dealt with are intracranial aneurysms—ruptured and unruptured—and epilepsy.

Apart from the irritating placing of illustrations, the book is well produced on paper many a British medical author (surgeons are always better served in this respect than physicians) might envy, and the photographs, though superabundant, are excellently produced.

Far too few of the present generation of neurologists read German and perhaps events have conspired to make it seem less necessary to do so now than a quarter of a century ago—perhaps also this work with its complete lack of literary graces and fluency is a forbidding introduction to this language. Nevertheless, this is a valuable work of reference from the very weight of information it contains—not, it is true, information on electrophysiology or electronics, but upon clinical neurology and neuropathology which will remain the foundations of our discipline as long as we remain physicians. Therefore, despite the fact that in the chapter on epilepsy, electroencephalography is dismissed in a brief paragraph, without a reproduced record, this book will justify a place in the neurologist's library.

F. M. R. W.

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Doubt and Certainty in Science: A Biologist's Reflections on the Brain. (Reith Lectures 1950). By J. Z. Young. Clarendon Press, Oxford. Price 7s. 6d.

The explanatory subtitle of these lectures, to each of which the author in this volume appends a lengthy commentary, gives a most misleading impression of the range of their contents.

There is scarcely a subject from theology, cosmology and genetics to physics and mathematics upon which some *ex cathedra* view is not expressed. For example, we read "there is not much sense any more in speaking of beginnings or endings, or of 'creation.' "

In what sense this airy *obiter dictum*, and many others like it, can be called a biological reflection on the brain will be less apparent to his readers than to Professor Young. Yet the lectures abound in just such flights.

The author sides with those who call the mind a "pseudo-thing." The terms "idea" and "concept" are thus logically barred to him and he replaces them, when he remembers to do so, by such clumsy locutions as "rules of action laid down in the brain" and "models in the brain." But the strain of this verbal tight-rope walking proves too much, and here and there creep in such terms as "idea," "understanding" and "we understand"; though what place they can have in the grammar he claims to be adopting, is not at all clear.

For Professor Young the really essential quality of man in the animal kingdom, and he may hope for no other kingdom, is his power to communicate. For the author speech is simply a matter of signalling, of "information output." Emotive speech he does not recognize, though it is impossible to conceive of human speech without it.

This theme of communication is a main one and leads to one of Professor Young's most naïve self-revelations. The fifth lecture opens dramatically with a page of largely emotive speech in which he relates a visit to the cathedral of Notre Dame in Paris while these lectures were in course of composition. "As I looked up at the tremendous vertical lines of the nave," he says, "I found that there were tears in my eyes."

"Why," he goes on to ask, "is it that one is sometimes moved in this way by a great church?" What is its significance in terms of human survival? Whence this human habit of making great buildings? His astonishing answer is that churches "form a link in the process of ensuring communication. They play an essential part in establishing the rules of brain action that make co-operation possible." This profound conclusion reminds us of our dependence upon others, and this in its turn elicits one of our earliest responses—crying. Here, surely, is pure bathos.

The builders of Notre Dame, who may be presumed to have known what they intended, would have given another answer: one that Professor Young, who expressly rejects the mediæval concept of the universe and of man, would not understand, for it would not fit the rules of action laid down in his brain.

They would have said that they were not primarily concerned with human survival, for they believed that man has here no abiding city, and they would have added that beneath its vault they met to raise their minds and hearts to God, and not to communicate with one another. This may have been very childish of them; Professor Young would certainly think so, but we may well ask ourselves whether the weight of childishness in this matter rests with the mediæval or with the modern view, in so far as Professor Young reflects the latter. Men have died for the mediæval view, but no scientific martyr will ever go to the stake for the principle of "communication."

One thing is crystal clear, that Professor Young's doubts are many men's certainties, as his certainties are many men's doubts.

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Yet we must not despair of him, for, after all, he did shed tears in a cathedral, though few readers will find it possible to believe that it was the mere idea of "communication" that so moved him. Surely, down in the tangled forest of his abstractions something still human stirred, something with ancient roots that he has been unable to expel with his mathematical pitchfork.

The threads upon which Professor Young strings his soliloquies upon this and that include the notion—if the obsolete word may be pardoned—that the brain is a vastly complex computor, and the chill belief that we shall achieve a satisfactory picture of ourselves only in "an elaborate statistical and mathematical terminology." Cybernetics seems to be the light by which he travels hopefully towards this soulless and exsanguinated concept of the human person in which nothing biological remains.

Can we really accept all this as the expression of an evolutionary biology, one in which all that remains of man are the mathematical ashes left by his dialectical dissolution and cremation?

It has to be said, however, that these lectures contain a vast amount of information culled from many scientific disciplines, and in this sense they are a *tour de force*. Yet a man cannot be a universal scientist, and for the greater part of his thought he is dependent upon common sense, and if this fails him he is in a sad plight when he undertakes all that is attempted in these ambitious lectures.

They are couched in what we must suppose the author deemed to be a popular conversational style, meet for the vulgar. It is not the vulgar who will read through them to the end, but the cultivated, and these will suffer repeated shocks from the very careless English in which they are written.

For example, we read that "wild animals mostly co-operate seldom"; that "the word (sic) atom or electron is not used as the name of a piece. It is used as part of the description of the observations of physicists. It has no meaning except as used by people who know the experiments by which it (sic) is revealed. The results of these experiments are nothing more than relations between measurements expressed in mathematical formulæ." What could be more clear? And, finally, "Every race (sic) of plant, animal, or man, maintains its organization by taking in food, water and oxygen. With the energy provided, by these it does work of various kinds to keep itself intact." Modern improved communication certainly seems very hard going.

A writer who cannot manage the pronoun "it," and who seems at times unable to construct a coherent sentence, is in an anomalous situation when he ventures to praise the powers of communication our new brain models provide for us. Perhaps the ancients, with their simpler brain models, could have given us something more elegant and lucid, for these childish folk did know their grammar.

As we labour through these pages there come to mind the apt lines of Boileau,

'Avant donc que d'écrire apprenez à penser;

. . . . . .

Ce que l'on conçoit bien s'énonce clairement,

Et les mots pour le dire arrivent aisément.'

It remains to ask whether the prestige of science and of scientists in the mind of the educated layman can be enhanced by the publication of these lectures in their present form, or could survive the appearance of many more like them.

F. M. R. W.

FIRST INTERNATIONAL MEETING OF NEUROPATHOLOGISTS

to be held in Rome

from September 8 to 13, 1952

President: Dr. Mario Gozzano (Rome).

Secretary General: Dr. Armando Ferraro (New York).

Final arrangements are now being made for the programme of this morning. It has been decided that the following subjects should be discussed one day being devoted to each subject.

I Histopathology of the demyelinating diseases.
II Histopathology of vascular diseases.
III Histopathology of schizophrenia.
IV Histopathology of mental deficiencies.
V Histopathology of senility.

In addition, part of one or more days will be devoted to short papers of special interest not related to the above subjects and to cinematographic and microscopical demonstrations.

The British Committee will be glad to receive offers of short papers for this meeting, especially of papers related to the five main topics. Those who wish to read papers should communicate with Dr. J. G. Greenfield at the National Hospital, Queen Square, London, W.C.1, or with any member of the British Committee, giving the full title of the paper, along with a summary showing in what respects it covers new ground.

British Committee: Dr. J. G. Greenfield, Hon. President; Prof. Dorothy S. Russell, Vice-President; Prof. J. H. Biggart; Dr. W. Blackwood; Dr. W. H. McMenemey; Prof. A. Meyer; Dr. R. M. Norman.

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FOR

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